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Evaluation of RSDL, M291 SDK, 0.5% Bleach, 1% Soapy Water and SERPACWA:

Part 11: Challenge with EA4243 (VR, Russian VX)

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14. ABSTRACT An important objective of the Project Solicitation for Agent Therapeutics (Task Area 2.H) was to determine the effectiveness of current medical countermeasures against the acute toxicity of nerve agents. This project evaluated the efficacy of skin decontamination products and barrier skin creams. Doctrine described the use of Skin Exposure Reduction Paste Against Chemical Warfare Agents (SERPACWA) as a barrier skin cream and the M291 Skin Decontamination Kit (SDK), 0.5% hypochlorite solution (household bleach diluted 1 to 10) and 1% soapy water solution (liquid dish detergent) to decontaminate intact skin exposed to chemical warfare agents. Reactive Skin Decontamination Lotion (RSDL) was approved by the FDA in 2003 and subsequently selected as the Joint Services Personnel Skin Decontamination System (JSPDS) to replace the M291 SDK. This report, the eleventh in a series, directly compares the efficacy of the barrier skin cream SERPACWA and the four listed decontamination products in the haired guinea pig model following exposure to VR (Russian VX, EA4243).					
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EXECUTIVE SUMMARY

An important objective of the Project Solicitation for Agent Therapeutics (Task Area 2.H) was to determine the effectiveness of current medical countermeasures against the acute toxicity of nerve agents. This project evaluated the efficacy of skin decontamination products and barrier skin creams. Doctrine described the use of Skin Exposure Reduction Paste Against Chemical Warfare Agents (SERPACWA) as a barrier skin cream and the M291 Skin Decontamination Kit (SDK), 0.5% hypochlorite solution (household bleach diluted 1 to 10) and 1% soapy water solution (liquid dish detergent) to decontaminate intact skin exposed to chemical warfare agents. Reactive Skin Decontamination Lotion (RSDL) was approved by the FDA in 2003 and subsequently selected as the Joint Services Personnel Skin Decontamination System (JSPDS) to replace the M291 SDK. This report, the eleventh in a series, directly compares the efficacy of the barrier skin cream SERPACWA and the four listed decontamination products in the haired guinea pig model following exposure to VR (Russian VX, EA4243).

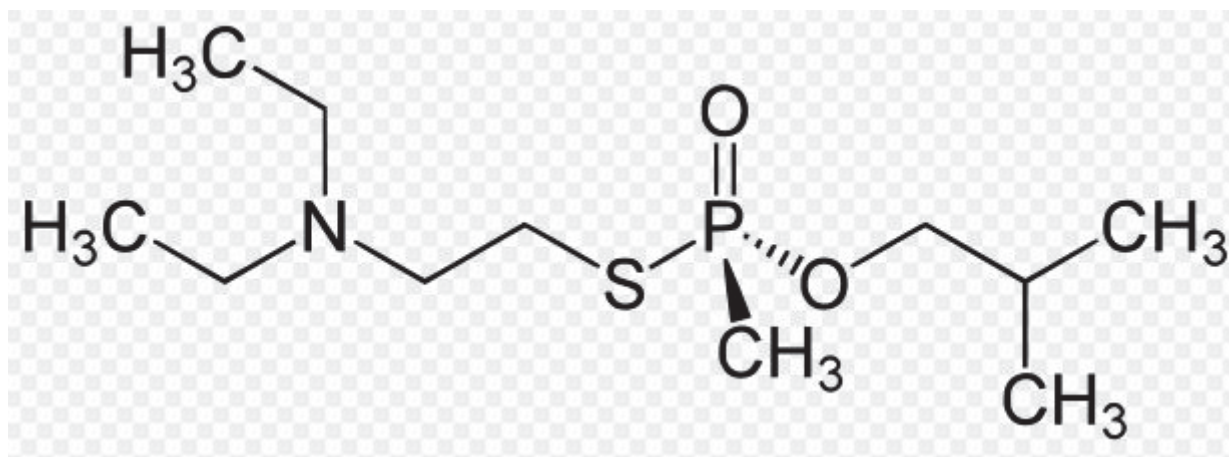
In all experiments, guinea pigs were close-clipped and given anesthesia (ketamine and xylazine). SERPACWA was applied as a thin coating (0.1 mm thick), allowed to dry for 15 minutes and challenged with VR. After a 2-hour challenge any remaining VR was blotted off the animal, but no additional decontamination was done. In decontamination experiments, the animals were challenged with VR and decontaminated after a 2-minute delay for the standard procedure or at longer times for the delayed-decontamination experiments. Positive control animals were challenged with VR in the same way as the treated animals except that they received no treatment. In addition, positive control animals always were challenged with 5% VR in isopropyl alcohol (IPA) solution, whereas the treatment animals received either neat VR or 5% VR in IPA solution. All animals were observed during the first 4 hours and again at 24 hours postexposure for signs of toxicity and death. The protective ratio (PR, defined as LD_{50} of the treatment group divided by the LD_{50} of the untreated positive control animals) was calculated from the derived median lethal dose-response curve parameters established for each treatment group and non-treated control animals. Significance in this report was defined as $p < 0.05$ unless otherwise stated.

The results showed that SERPACWA provided modest protection against neat VR with a PR value (95% confidence interval, CI) of 3.2 (1.7, 6.1). In the standard 2-minute decontamination experiments the calculated PR values (95% CI) for 0.5% bleach, M291 SDK, RSDL, and 1% soapy water were **60** (38, 92), **1.0** (0.74, 1.5), **140** (88, 221), and **27** (16, 45), respectively. RSDL, bleach (0.5%) and soapy water (1%) provided significant protection, but the M291 SDK provided no increased protection. RSDL was by far the most effective decontamination product tested and significantly better than any of the other products. Bleach (0.5%) was significantly better than soapy water (1%) and the M291 SDK. Soapy water (1%) was significantly better than the M291 SDK.

In the neat VR delayed-decontamination experiments, the estimated LT_{50} (95% CI) values (the delayed-decontamination time where 50% of the animals died in the test population following a 5 LD_{50} challenge dose of 1.06 mg/kg) for bleach (0.5%), RSDL, and soapy water (1%) were **22** (13, 32), **69** (53, 84), and **24** (12, 42) minutes, respectively. These results indicated that there is a window of opportunity for effective decontamination. For VR, the window for effective decontamination ranged from 22 to 69 minutes depending on the decontamination product used. A more preferable time, however, is the time in which few deaths are expected. The 10% lethality delay times (95% CI) for bleach, RSDL, and soapy water were 13 (2.3, 19), 53 (18, 63), and 9.3 (0.83, 16) minutes, respectively.

INTRODUCTION

This report, the eleventh in a series, directly compares the efficacy of the four listed decontamination products and SERPACWA in the haired guinea pig model following exposure to VR (Russian VX, EA4243, Soviet V-gas, Substance 33, R33, (N,N-diethyl-2-(methyl-(2-methylpropoxy)phosphoryl)sulfanylethanamine). Part 1 of the series (Braue et al., 2009) provided a detailed introduction to the decontamination products, SERPACWA, and the nerve agents, as well as to the threat nerve agents represent for warfighters and the civilian population.



VR (Russian VX, EA4243)

OBJECTIVE

The first objective of this study was to determine the efficacy of four decontamination products in guinea pigs challenged with VR: 0.5% bleach, the M291 SDK, Reactive Skin Decontamination Lotion (RSDL), and 1% soapy water. The second objective was to determine how the efficacy was affected by delaying application of these decontamination products following challenge with VR. The third objective was to determine the efficacy of the pretreatment barrier skin cream SERPACWA challenged with VR.

MATERIALS AND METHODS

A detailed description of the experimental methods used for this project may be found in the first published manuscript in the series (Braue et al., 2009). In all experiments, guinea pigs were close-clipped and given anesthesia (ketamine and xylazine). SERPACWA was applied as a thin coating (0.1 mm thick, over 7.1 cm²), allowed to dry for 15 minutes and challenged with VR. After a 2-hour challenge any remaining VR was blotted off the animal, but no additional decontamination was done. In decontamination experiments, the animals were challenged with VR and decontaminated after a 2-minute delay for the standard procedure or at longer times for the delayed-decontamination experiments. Positive control animals were handled in the same manner as the treated animals except that they received no treatment. In addition, positive control animals always were challenged with 5% VR in isopropyl alcohol (IPA) solution, whereas the treatment animals received either neat VR or 5% VR in IPA solution. All animals were observed during the first 4 hours and again at 24 hours postexposure for signs of toxicity and death. The protective ratio (PR, defined as LD₅₀ of the treatment group divided by the LD₅₀ of the untreated positive control animals) was calculated from the derived median lethal dose-response curve parameters established for each treatment group and non-treated control animals. Significance in this report was defined as $p < 0.05$ unless otherwise stated.

These experiments were conducted between 20 September 2004 and 9 September 2010. A 100% quality control audit was conducted by team members to verify that all data were correctly transcribed from the laboratory notebook to the Excel data base.

Agent Application

VR (Russian VX, EA4243, Soviet V-gas, Substance 33, R33, (N,N-diethyl-2-(methyl-(2-methylpropoxy)phosphoryl)sulfanylethanamine, O-isobutyl-S-[(2-diethylamino) ethyl] methylphosphonothiolate) was obtained from the U.S. Army Edgewood Chemical Biological Center (ECBC), Aberdeen Proving Ground, MD. The experiments conducted at the U.S. Army Medical Research Institute of Chemical Defense (USAMRICD) cover three time frames and three different lots were received. The experiments conducted between Jan 2005 through Jan 2006 used lot number 04.0011.39 with a purity of 93.4% determined by NMR spectroscopy. The experiments conducted 11-18 September 2008 used lot number 04.0011.69.1 with a purity of 94.5% determined by NMR spectroscopy. The experiments conducted in August and September 2010 used lot number 04.0011.171 with a purity of 95.0% determined by NMR spectroscopy. The experiments conducted at Battelle between 20 September 2004 and 2 November 2004 used VR, obtained from the Army, with a purity of 78.1%. The VR used at Battelle was less pure than the experiments conducted at the USAMRICD, but Battelle corrected for purity in their calculations.

VR was applied to the marked area on the animal (side for decontamination and back for SERPACWA) using one of various pipetting devices, depending on the volume needed. Volumes smaller than 2.0 microliters (μ l) used either a Rainin micropipette (P-

2, Rainin Instrument, LLC, Oakland, CA 94621) or a Hamilton microsyringe (0.5, 1, 5 μ l, The Hamilton Co., Reno, NV 89502). Experiments that required volumes greater than 2.0 μ l used a Rainin micropipette (P-10, P-20, P-100, P-200, P-1000) or a Drummond positive displacement microdispenser (10, 25, 50, 100, 1000 μ l, The Drummond Scientific Co., Broomall, PA 19008). Either neat VR or a 5% VR IPA solution was applied. The initial experiments at the USAMRICD used neat VR whenever the challenge dose required a volume greater than or equal to 0.5 μ l and a 5% VR IPA solution when the volume was less than 0.5 μ l. This decision was made to minimize the pipetting uncertainties in precision and accuracy inherent in trying to deliver sub-microliter volumes with a pipette. This pipetting decision resulted in all positive control animals (animals receiving VR but no treatment), animals decontaminated with the M291 SDK, and a few animals decontaminated with either 0.5% bleach or 1% soapy water being challenged with 5% VR IPA solution. All of the animals decontaminated with RSDL and most of the animals decontaminated with 0.5% bleach or 1% soapy water were challenged with neat VR. The M291 SDK evaluation was later repeated with neat VR challenge.

At least once per week quality control (QC) samples of VR were prepared by pipetting 9.5 μ l of neat VR into a 10 ml volumetric flask and adding chloroform to the fill line. The diluted sample of VR was analyzed by a gas chromatography (GC) system (HP model 6890) using a flame ionization detector (FID). If any sample concentration was outside three standard deviation units from the study mean the data for that day were omitted.

Experiments evaluating SERPACWA were conducted under contract with Battelle Memorial Institute (Snider et al., 2005). The procedures used by Battelle to evaluate the efficacy of SERPACWA (ICD # 3004) were the same as used by the USAMRICD for the other nerve agents in the series, except neat VR was used to challenge positive control animals. The Battelle experiments were conducted between 20 September 2004 and 2 November 2004. The details and results were reported in the contract final report dated 15 July 2005.

Data Analysis

Statistical analysis of the data from these experiments was performed using SAS software, version 6.12 (SAS Institute, Inc., Cary, NC 27513). Data sets were analyzed using specialized probit analysis programs for a stage-wise adaptive dose design (Feder, 1991) written using SAS NLIN to estimate the LD₅₀ and 95% confidence interval (CI). The PROBSEP program (Braue et al., 2009, Appendix B) produced a great deal of statistical information (see APPENDIX B: SAS ANALYSIS OUTPUT FILES for complete listing), but only a small portion will be given in the tables including LD₁₀, LD₅₀, and LD₉₀ values with lower and upper 95% CIs based on Fieller's method (Finney, 1971), and the probit slope. An additional specialized program using SAS, called PRORATIO (Braue et al., 2009, Appendix C), used the output from the SAS PROBSEP program to calculate the PR of each of the treatments compared to the positive controls and to each of the other treatment groups. The PRORATIO program also estimated a

confidence interval for the PR (using the delta method, Nelson, 1982), which was used to determine whether the PR was significant and therefore whether the LD₅₀ values of the groups were significantly different. Statistical significance was defined as $p < 0.05$ unless otherwise stated.

The reported SAS analysis output for each treatment group used animals challenged with either neat VR or a 5% IPA solution of VR. The raw data tables for animals decontaminated with 0.5% bleach and 1% soapy water lists a few animals that were challenged with a 5% IPA solution of VR, but these animals were not included in the SAS analysis (see discussion).

RESULTS

In Appendix A, Tables A1-A5 provide the raw data for the standard decontamination experiments (decontamination 2 minutes postexposure). These tables provide the 24-hour survival data for positive control animals and animals decontaminated with 0.5% bleach, M291 SDK, RSDL, and 1% soapy water. Five percent VR IPA solution was used for positive control animals and the first evaluation of the M291 SDK. Neat VR or 5% VR IPA solution were used for the other decontamination products as labeled.

In Appendix A, Tables A6-A7 provide the raw data for the SERPACWA experiments conducted at Battelle Memorial Institute. These tables provide the 24-hour survival data for positive control animals and for animals pretreated with SERPACWA. Neat VR was used for positive control and SERPACWA animals.

In Appendix A, Tables A8-A10 provide the survival raw data for the delayed-decontamination experiments. In delayed-decontamination experiments, the decontamination process was delayed from 2 to 180 minutes postexposure. All these animals were challenged with 1.06 mg/kg BW (body weight) representing a 5 LD₅₀ dosage as determined in the repeat VR experiments.

In Appendix A, Tables A11-A12 provide the raw data for the repeat experiments for the M291 SDK. These tables provide the 24-hour survival data for positive control animals and animals decontaminated with M291 SDK. Five percent VR IPA solution was used for positive control animals, and neat VR was used for animals decontaminated with M291 SDK.

Appendix B provides the SAS output files giving complete details of the data analysis.

Figure 1 is a graph of the LD₅₀ values for the four decontamination products and positive control animals in the guinea pig model. The error bars represent the 95% CI. The number of animals used per treatment group was between 18 and 50. In the first run, positive control and M291 SDK animals were challenged with a 5% VR IPA solution. The 0.5% bleach, RSDL, and 1% soapy water animals were challenged with neat VR. The efficacy evaluation of the M291 SDK was repeated using neat VR for the

M291 SDK animals and a 5% VR IPA solution for the positive control animals. The LD₅₀ values (95% CI) for positive control, positive control repeat, 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **0.134** (0.093, 0.198), **0.212** (0.137, 0.299), **7.98** (4.75, 16.8), **0.211** (0.084, 0.350), **0.221** (0.150, 0.291), **18.7** (10.9, 30.2), and **3.57** (1.01, 5.76) mg/kg BW, respectively.

Figure 2 contains dose-response curves for decontamination products in the guinea pig model. Five percent VR IPA solution or neat VR was used for control and decontamination products as labeled. LD₅₀ values (mg/kg BW) are given in the text blocks. Dose-response curve slopes (95% CI) for positive controls, positive controls repeat, 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **9.03** (0.124, 17.9), **5.51** (1.05, 9.87), **3.14** (0.526, 5.76), **2.75** (0.413, 5.08), **7.58** (1.31, 13.8), **2.13** (0.881, 3.38), and **2.54** (0.453, 4.62), respectively.

Figure 3 is a graph of the PR values with respect to the positive controls. The PR values (95% CI) for 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **59.5** (38.4, 92.2), **1.57** (0.998, 2.48), **1.04** (0.735, 1.48), **140** (88.8, 221), and **26.6** (15.7, 45.2), respectively. PR values with the same letter were not significantly different. RSDL, 0.5% bleach, and 1% soapy water provided significant protection.

The SERPACWA efficacy evaluations were conducted by Battelle Memorial Institute. The LD₅₀ values (95% CI) for control and SERPACWA were **0.733** (0.663, 0.796) and **2.35** (1.28, 5.71) mg/kg BW, respectively. The dose-response curve slopes (95% CI) for control and SERPACWA were **23.5** (7.95, 39.0) and **1.73** (0.837, 2.62), respectively. The number of animals used for positive control and for SERPACWA animals was 47 and 48, respectively. All animals were challenged with neat VR. The PR value (95% CI) of SERPACWA was **3.20** (1.69, 6.08) and was significant.

Figure 4 is a graph of percent lethality when 0.5% bleach, RSDL, or 1% soapy water decontamination was delayed following challenge by 1.06 mg/kg (5 LD₅₀s) of neat VR. A total of 25, 31, and 26 animals were used with bleach, RSDL, and soapy water, respectively. The LT₅₀ (50% lethality time) values (95% CI) for 0.5% bleach, RSDL and 1% soapy water were **22.0** (12.6, 32.2), **68.9** (53.1, 84.1), and **23.9** (12.1, 42.3) minutes, respectively. The dose-response curve slopes (95% CI) for 0.5% bleach, RSDL and 1% soapy water were **5.85** (1.15, 10.5), **11.2** (1.17, 21.2), and **3.13** (0.788, 5.48), respectively.

Tables 1-3 provide a summary of the SAS probit analysis for all of the experiments. It consists of, for each treatment, the number of animals, the LD₁₀, LD₅₀ and LD₉₀ (LT₁₀, LT₅₀ and LT₉₀ for delayed-decontamination experiments), the lower and upper 95% CI, the dose-response curve slope, and the PR. The delta method was used to calculate confidence intervals for PRs and to determine which were significantly different.

AGENT	No. of G.P.	Treat-ment	LD ₅₀ mg/kg (95% C.I.)	Slope (95% C.I.)	PR (95% C.I.)	Sig p < 0.05	LD ₁₀ mg/kg (95% C.I.)	LD ₉₀ mg/kg (95% C.I.)
VR Sol'n	18	Control	0.134 (0.093 - 0.198)	9.03 (0.124 - 17.9)	1.00	a, c	0.097 (0.009 - 0.119)	0.186 (0.151 - 2.13)
VR Neat	27	Bleach	7.98 (4.75 - 16.8)	3.14 (0.526 - 5.76)	59.5 (38.4 - 92.2)	b	3.12 (0.168 - 5.08)	20.4 (11.9 - 627)
VR Sol'n	31	M291	0.211 (0.084 - 0.350)	2.75 (0.413 - 5.08)	1.57 (0.998 - 2.48)	c, a	0.072 (0.001 - 0.130)	0.619 (0.366 - 24.0)
VR Neat	50	RSDL	18.7 (10.9 - 30.2)	2.13 (0.881 - 3.38)	140 (88.2 - 221)	d	4.69 (0.676 - 8.77)	74.8 (41.7 - 438)
VR Neat	32	Soap	3.57 (1.01 - 5.76)	2.54 (0.453 - 4.62)	26.6 (15.7 - 45.2)	e	1.12 (0.009 - 2.28)	11.4 (6.74 - 243)
VR Sol'n	27	Control Repeat	0.212 (0.137 - 0.299)	5.51 (1.15 - 9.87)	1.00	f, g	0.124 (0.030 - 0.172)	0.362 (0.267 - 1.22)
VR Neat	32	M291 Repeat	0.221 (0.150 - 0.291)	7.58 (1.31 - 13.8)	1.04 (0.735 - 1.48)	g, f	0.150 (0.038 - 0.193)	0.326 (0.260 - 1.00)

Table 1. Data summary of efficacy experiments for decontamination products with animals challenged with VR. Five percent VR IPA solution or neat VR was used for control and decontamination products as labeled. Data includes standard 2-minute decontamination experiments from 5 January 2005 to 24 February 2005 and for the M291 SDK repeat experiments, 10 - 19 January 2006 (Tables A1 – A5 and A11 - A12).

AGENT	No. of G.P.	Treatment	LT₅₀ min (95% C.I.)	Slope (95% C.I.)	Sig p < 0.05	LT₁₀ min (95% C.I.)	LT₉₀ min (95% C.I.)
VR Neat	25	Bleach delayed	22.0 (12.6 - 32.2)	5.85 (1.15 - 10.5)	a, c	13.3 (2.28 - 18.8)	36.4 (26.6 - 145)
VR Neat	31	RSDL delayed	68.9 (53.1 - 84.1)	11.2 (1.17 - 21.2)	b	52.9 (17.7 - 62.6)	89.8 (76.8 - 234)
VR Neat	26	Soap delayed	23.9 (12.1 - 42.3)	3.13 (0.788 - 5.48)	c, a	9.30 (0.834 - 16.0)	61.2 (36.6 - 537)

Table 2. Data summary of efficacy experiments for delayed decontamination with animals challenged with 1.06 mg/kg BW neat VR (5 LD₅₀s). Data includes delayed-decontamination experiments from 11-18 September 2008 and 31 August 2010 to 9 September 2010 (Tables A8 – A10).

AGENT	No. of GP	Treatment	LD ₅₀ mg/kg (95% C.I.)	Slope (95% C.I.)	PR (95% C.I.)	Sig p < 0.05	LD ₁₀ mg/kg (95% C.I.)	LD ₉₀ mg/kg (95% C.I.)
VR Neat	47	Control	0.733 (0.663 - 0.796)	23.5 (7.95 - 39.0)	1.00	a	0.646 (0.491 - 0.699)	0.831 (0.772 - 1.05)
VR Neat	48	SERPACWA	2.35 (1.28 - 5.71)	1.73 (0.837 - 2.62)	3.20 (1.69 - 6.08)	b	0.425 (0.090 - 0.837)	13.0 (5.42 - 129)

Table 3. Data summary of efficacy experiments for SERPACWA with animals challenged with neat VR. Data includes

SERPACWA experiments from 20 September 2004 to 2 November 2004 (Tables A6 – A7). These experiments were conducted at Battelle Memorial Institute.

Notes for Tables 1-3:

- LD₁₀, LD₅₀, and LD₉₀ = the dosage (mg/kg BW) required to kill 10, 50, and 90%, respectively, of the test population by 24 hours postexposure (95% CI using Fieller's method).
- LT₁₀, LT₅₀, and LT₉₀ = the delayed-decontamination time at which 10, 50, and 90% of the animals in the test population die by 24 hours postexposure (95% CI using Fieller's method).
- PR = Protective ratio (LD₅₀ of treatment/LD₅₀ of control) with 95% CI using the delta method.
- Sig = Protective ratios with same letter were not significantly different (p < 0.05) using the delta method.
- Slope = The slope of the dose-response curve with 95% CI using Fieller's method.

DISCUSSION

Decontamination Efficacy Experiments

The four decontamination products evaluated can be divided into two categories based on cost and use. The M291 SDK and RSDL are relatively expensive (the RSDL packet costs about \$20 and the M291 SDK cost about \$3.35) and designed to be carried by individuals for immediate lifesaving spot decontamination on small intact skin areas following exposure. The U.S. military began to phase out the use of the M291 SDK in 2008 and it is no longer commercially available. On the other hand, 0.5% bleach and 1% soapy water are relatively inexpensive and generally used for whole body decontamination of an exposed person prior to moving the individual from a dirty zone into a clean zone. All four of these products were described in U.S. doctrine for CWA decontamination of intact skin; however, a comprehensive evaluation comparing the efficacy of these products was never accomplished prior to this study. This technical report is the eleventh in a series to provide a comprehensive comparison of the efficacy of these decontamination products and SERPACWA against many of the traditional agents and other toxic compounds.

The real world threat scenario is for exposure to neat agent not agent in solution. The toxicity of nerve agents was so great, however, that the dosage volumes required to cover the full range of the dose-response curve for untreated animals were too small to be pipetted reliably. Initially, the decision was made to minimize the pipetting uncertainties in precision and accuracy by using neat agent only whenever the challenge dose required a volume greater than or equal to 0.5 μl .

During the evaluation of toxic compounds, we discovered that the efficacy of a decontamination product can be greatly affected by whether the agent is neat or in solution. We observed that the decontamination products were significantly less effective for animals challenged with agent in solution than when the agent was neat. We theorized that this observation resulted from the solvent increasing the systemic uptake of agent by changing the barrier function of the skin and by spreading the agent over a larger skin area thus making the decontamination process less effective. These observations caused us to re-think our decision to use agent in solution when evaluating cutaneous treatments. Following this analysis, the decision was made in November 2005 to use only a neat agent challenge for evaluating skin treatments in all future experiments. We also made the decision to re-evaluate the M291 SDK using neat VR challenge instead of 5% VR IPA solution. We recognized that trying to pipette very small volumes (0.05 to 0.5 μl) could not be accomplished with a high degree of accuracy or precision. We decided it was better to use neat agent and accept this uncertainty than to generate unreliable data from using agent in solution. The uncertainty in delivering these very small volumes was mitigated to some degree by using more animals for each experiment. For positive control animals, which received no treatments, agent in solution was still used if the required volume was < 0.5 μl . The rationale for this decision was that the agent had 24 hours to reach the systemic

circulation; thus a modified penetration rate should not significantly affect the observed 24-hour lethality.

In the standard 2-minute decontamination experiments the calculated PR values (95% CI) for 0.5% bleach, M291 SDK (neat), RSDL, and 1% soapy water were **60** (38, 92), **1.0** (0.74, 1.5), **140** (88, 221), and **27** (16, 45), respectively. RSDL, bleach (0.5%) and soapy water (1%) provided significant protection, but the M291 SDK provided no increased protection. RSDL was by far the most effective decontamination product tested and significantly better than any of the other products. Bleach (0.5%) was significantly better than soapy water (1%) and the M291 SDK. Soapy water (1%) was significantly better than the M291 SDK. The M291 SDK efficacy did not improve in the repeat experiments using a neat VR challenge. The PR value (95% CI) in the repeat experiment was only **1.04** (0.735, 1.48) and not significantly different from untreated control animals.

The LD₅₀ value is traditionally used to compare the toxicity of chemicals; however, the dose-response curve slope is also an important parameter to indicate how quickly the percent lethality changes with applied dose. If the dose-response curve slope is flat, the percent of lethality changes very slowly with changes in dose, and a significant percentage of deaths are observed at doses far removed from the LD₅₀ dose. The PROBSEP program run in SAS to analyze this data set not only provided the LD₅₀ values but also gave doses for the complete range of lethality percentiles including 1, 10, 16, 30, 50, 70, 84, 90, and 99. The doses for this entire range are listed in the SAS output files recorded in Appendix B. Table 1 provides the slope, LD₁₀, LD₅₀, and LD₉₀ values along with the 95% CI values so that the reader can fully understand the toxicity of VR and the effectiveness of the products tested.

In a real-life scenario, warfighters or civilians may not realize that they have been contaminated with a toxic agent. Thus, they may not start the decontamination process until well after the recommended time of 1 or 2 minutes postexposure. The conventional wisdom for many years was that decontamination would only be effective if performed in the first few minutes after exposure. When this study started in 2005, no comprehensive evaluations were available on the effectiveness of decontamination products beyond the standard 2-minute delay time. A limited study (Hamilton et al., 2004) using only 3 animals per treatment group evaluated VX decontamination with RSDL in swine (Yorkshire-Landrace cross, 20 kg). In the Hamilton et al. study, RSDL was found to be significantly effective 15 minutes postexposure for neat VX challenge to the ear but not significantly effective 30 or 60 minutes postexposure for neat VX challenge to the epigastrium (belly). Recognizing the need for a comprehensive study, the scope our current study was expanded to include delayed-decontamination studies.

A fixed neat VR challenge dose of 1.06 mg/kg BW (5 LD₅₀) was used for all VR delayed-decontamination studies. This value was based on the results for the positive control animals in the M291 SDK repeat experiments. We used a 5 LD₅₀ challenge because historically a 5 LD₅₀ dose was the suggested minimum target for therapeutics selected for fielding. The lethality delay time-response curves were generated using the

stage-wise adaptive dose design similar to the LD₅₀ dose-response studies using the delay time in place of the mg/kg dose. The SAS probit analysis program was used to find the lethality percentiles associated with a given decontamination delay time. The LT₁₀, LT₅₀, and LT₉₀ values were defined as the delayed-decontamination times at which 10, 50, and 90% of the animals in the test population died following a 1.06 mg/kg (5 LD₅₀) challenge. A PR of 5, which is directly related to protection from a 5 LD₅₀ challenge, was the decision criteria for choosing the decontamination products for the delayed-decontamination experiments. Any decontamination products with a PR > 5 would be evaluated for delayed decontamination. For the VR experiments RSDL, 0.5% bleach, and 1% soapy water met this requirement. The M291 SDK with a PR of only 1.04 (neat or 1.57 [solution]) was omitted from the delayed-decontamination experiments.

In the neat VR delayed-decontamination experiments, the estimated LT₅₀ (95% CI) values for bleach (0.5%), RSDL, and soapy water (1%) were **22** (13, 32), **69** (53, 84), and **24** (12, 42) minutes, respectively. Dose-response curve slopes (95% CI) for bleach (0.5%), RSDL, and soapy water (1%) were **5.8** (1.2, 10), **11** (1.2, 21), and **3.1** (0.79, 5.5), respectively. For VR, the window for effective decontamination ranged from 22 to 69 minutes depending on the decontamination product used. A more preferable time, however, is the time in which few deaths are expected. The 10% lethality delay times (95% CI) for bleach, RSDL, and soapy water were **13** (2.3, 19), **53** (18, 63), and **9.3** (0.83, 16) minutes, respectively.

SERPACWA Efficacy Experiments

SERPACWA provided modest protection against VR. The PR (95% CI) was **3.2** (1.7, 6.1). However, in 2009, the Department of the Army decided that there was no longer a requirement for SERPACWA, since the new JSLIST protective suit was reported to solve the problem of leaking at the junction points (neck, wrist, waist, and ankle). Thus, SERPACWA was removed from the Army's stockpile and destroyed. Since that time, new evidence has suggested that a barrier cream like SERPACWA may still be needed.

CONCLUSIONS

- RSDL provided superior protection against VR with a protective ratio of **140** and was significantly better than the other products tested.
- The relative order of decontamination efficacy against VR was RSDL > 0.5% bleach > 1% soapy water > M291 SDK.
- The M291 SDK did not provide significant protection against VR.
- The windows for 50 and 90% effective decontamination following percutaneous exposure from VR are 22 – 69 and 13-53 min minutes, respectively.
- Skin Exposure Reduction Paste Against Chemical Warfare Agents (SERPACWA) provides modest protection against VR with a protective ratio of 3.2.

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FIGURES

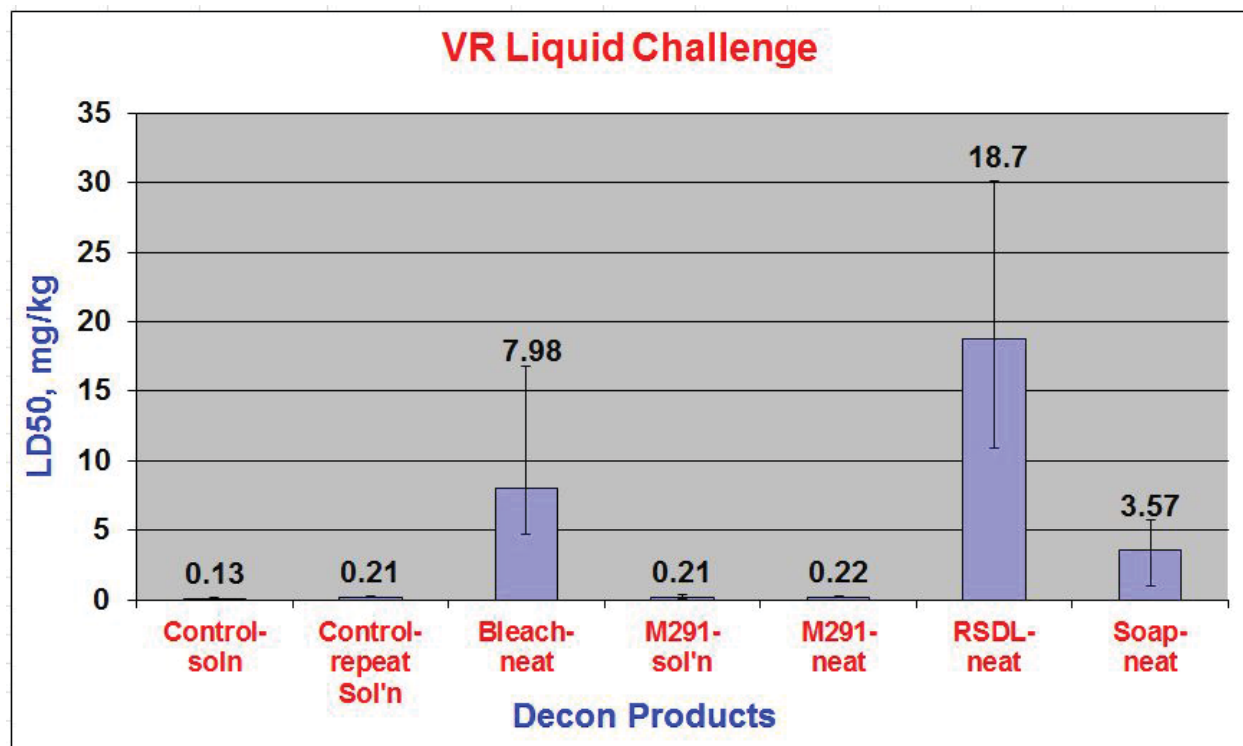


Figure 1. Graph of LD₅₀ values for decontamination products in guinea pig model. Error bars = 95% CI. The numbers of animals used per treatment group were 18 - 50. Animals were challenged with neat VR or 5% VR in IPA solution as labeled. The LD₅₀ values (95% CI) for positive control, positive control repeat, 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **0.134** (0.093, 0.198), **0.212** (0.137, 0.299), **7.98** (4.75, 16.8), **0.211** (0.084, 0.350), **0.221** (0.150, 0.291), **18.7** (10.9, 30.2), and **3.57** (1.01, 5.76) mg/kg BW, respectively.

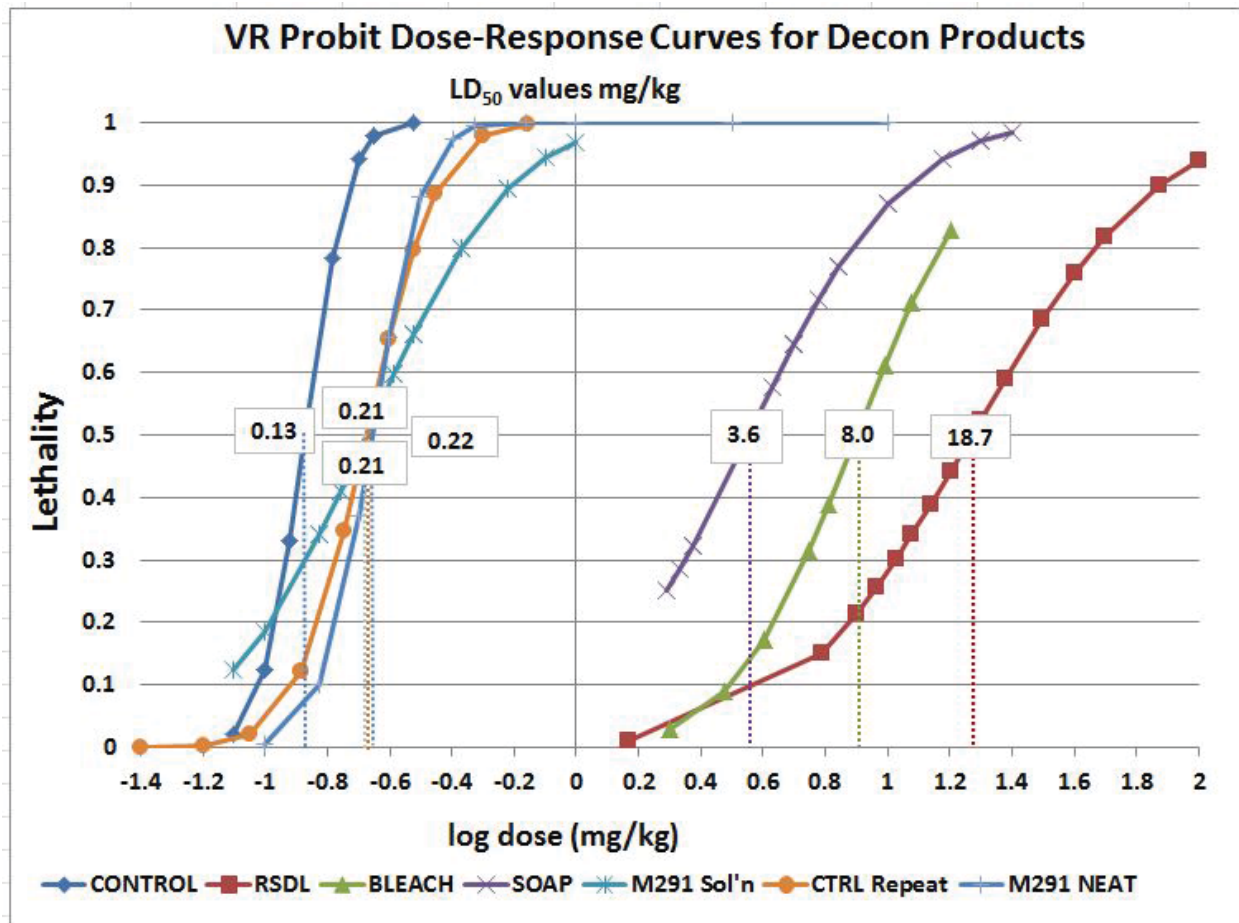


Figure 2. Dose-response curves for decontamination products in guinea pig model. Five percent VR in IPA solution was used for control, control repeat, and M291 SDK solution animals. Neat VR was used for RSDL, bleach, soap, and M291 SDK neat animals. LD₅₀ values (mg/kg BW) are given in text blocks. Dose-response curve slopes (95% CI) for positive controls, positive controls repeat, 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **9.03** (0.124, 17.9), **5.51** (1.05, 9.87), **3.14** (0.526, 5.76), **2.75** (0.413, 5.08), **7.58** (1.31, 13.8), **2.13** (0.881, 3.38), and **2.54** (0.453, 4.62), respectively.

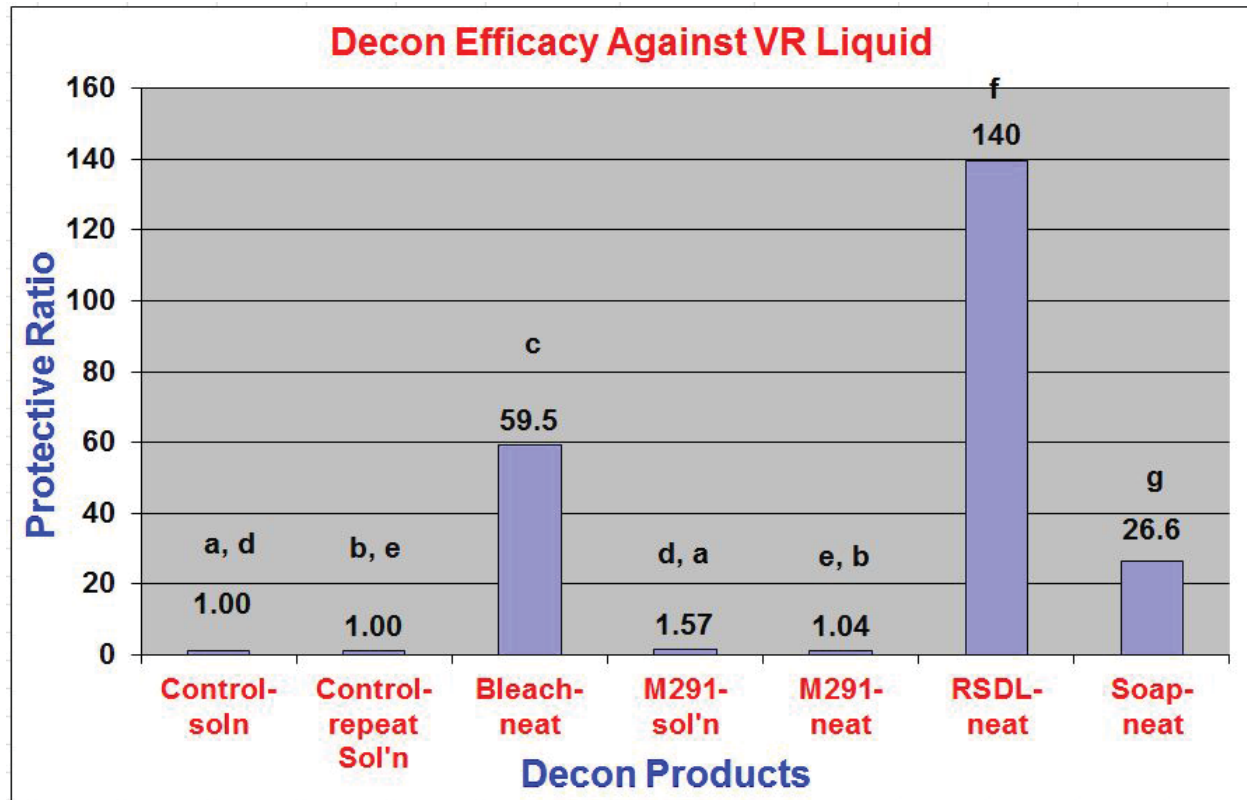


Figure 3. Graph of protective ratio (PR) values for decontamination products in guinea pig model. Animals were challenged with neat VR or 5% VR in IPA solution as labeled. The PR values (95% CI) for 0.5% bleach, M291 SDK solution, M291 SDK neat, RSDL, and 1% soapy water were **59.5** (38.4, 92.2), **1.57** (0.998, 2.48), **1.04** (0.735, 1.48), **140** (88.8, 221), and **26.6** (15.7, 45.2), respectively. PRs with same letter were not significantly different at $p < 0.05$. RSDL, 0.5% bleach, and 1% soapy water provided significant protection.

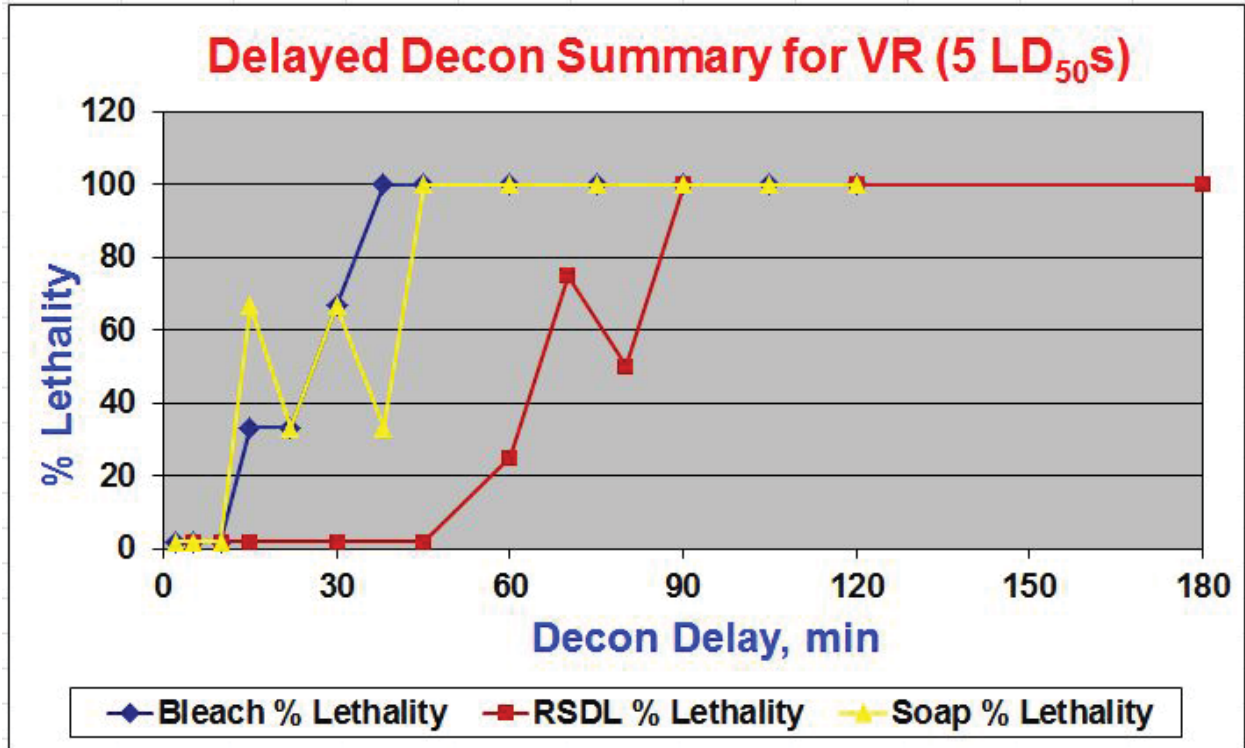


Figure 4. Graph of percent lethality when 0.5% bleach, RSDL, and 1% soapy water decontamination was delayed following challenge by 1.06 mg/kg (5 LD₅₀s) of neat VR. LT₅₀ (50% lethality time with 95% CI) for bleach, RSDL, and soapy water were **22.0** (12.6, 32.2), **68.9** (53.1, 84.1), and **23.9** (12.1, 42.3) minutes, respectively. The dose-response curve slopes (95% CI) for 0.5% bleach, RSDL and 1% soapy water were **5.85** (1.15, 10.5), **11.2** (1.17, 21.2), and **3.13** (0.788, 5.48), respectively.

APPENDIX A: EXPERIMENTAL RAW DATA

Agent	Date	Treatment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR IPA Sol'n	03-Feb-05	Control	0.080	-1.097	1	0	>24
VR IPA Sol'n	05-Jan-05	Control	0.100	-1.000	1	0	>24
VR IPA Sol'n	13-Jan-05	Control	0.100	-1.000	1	0	>24
VR IPA Sol'n	25-Jan-05	Control	0.120	-0.921	2	0	>24
VR IPA Sol'n	01-Feb-05	Control	0.120	-0.921	2	2	O/N, O/N
VR IPA Sol'n	11-Jan-05	Control	0.134	-0.873	1	1	O/N
VR IPA Sol'n	13-Jan-05	Control	0.134	-0.873	1	0	>24
VR IPA Sol'n	19-Jan-05	Control	0.134	-0.873	2	1	O/N, >24
VR IPA Sol'n	03-Feb-05	Control	0.164	-0.785	2	1	O/N, >24
VR IPA Sol'n	27-Jan-05	Control	0.200	-0.699	2	2	O/N, O/N
VR IPA Sol'n	11-Jan-05	Control	0.224	-0.650	1	1	O/N
VR IPA Sol'n	01-Feb-05	Control	0.224	-0.650	1	1	4
VR IPA Sol'n	05-Jan-05	Control	0.300	-0.523	1	1	O/N

Table A1. Raw data for positive control animals challenged with 5% VR IPA solution in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours).

Agent	Date	Treatment	Dose mg/k g	Log Dose	Number Animals	Number Dead	Time to Death
VR IPA Sol'n	03-Feb-05	Bleach	1.26	0.100	1	0	>24
VR IPA Sol'n	01-Feb-05	Bleach	1.58	0.199	1	1	O/N
VR Neat	25-Jan-05	Bleach	2.00	0.301	2	0	>24
VR Neat	27-Jan-05	Bleach	2.00	0.301	2	0	>24
VR Neat	17-Feb-05	Bleach	3.00	0.477	2	0	>24
VR Neat	05-Jan-05	Bleach	4.00	0.602	1	1	O/N
VR Neat	11-Jan-05	Bleach	4.00	0.602	1	1	O/N
VR Neat	13-Jan-05	Bleach	4.00	0.602	1	0	>24
VR Neat	10-Feb-05	Bleach	5.60	0.748	2	1	O/N, >24
VR Neat	17-Feb-05	Bleach	6.50	0.813	2	0	>24
VR Neat	05-Jan-05	Bleach	8.00	0.903	1	0	>24
VR Neat	11-Jan-05	Bleach	8.00	0.903	1	0	>24
VR Neat	13-Jan-05	Bleach	8.00	0.903	1	0	>24
VR Neat	08-Feb-05	Bleach	8.00	0.903	1	0	>24
VR Neat	03-Feb-05	Bleach	9.80	0.991	2	0	>24
VR Neat	08-Feb-05	Bleach	9.80	0.991	2	2	O/N
VR Neat	19-Jan-05	Bleach	12.0	1.079	2	2	4, O/N
VR Neat	01-Feb-05	Bleach	12.0	1.079	2	2	3, 3
VR Neat	15-Feb-05	Bleach	16.0	1.204	2	2	O/N

Table A2. Raw data for 0.5% bleach animals challenged with neat and 5% VR IPA solution in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours). SAS analysis only used neat animals.

Agent	Date	Treat- ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR IPA Sol'n	03-Feb-05	M291	0.080	-1.097	1	0	>24
VR IPA Sol'n	03-Feb-05	M291	0.100	-1.000	2	0	>24
VR IPA Sol'n	01-Feb-05	M291	0.150	-0.824	1	1	O/N
VR IPA Sol'n	15-Feb-05	M291	0.150	-0.824	2	0	>24
VR IPA Sol'n	01-Feb-05	M291	0.175	-0.757	2	2	4, O/N
VR IPA Sol'n	08-Feb-05	M291	0.175	-0.757	2	0	>24
VR IPA Sol'n	27-Jan-05	M291	0.200	-0.699	2	1	O/N, >24
VR IPA Sol'n	10-Feb-05	M291	0.200	-0.699	2	2	O/N, O/N
VR IPA Sol'n	13-Jan-05	M291	0.260	-0.585	2	0	>24
VR IPA Sol'n	25-Jan-05	M291	0.260	-0.585	2	2	O/N, O/N
VR IPA Sol'n	05-Jan-05	M291	0.300	-0.523	1	1	>24
VR IPA Sol'n	11-Jan-05	M291	0.300	-0.523	1	1	O/N
VR IPA Sol'n	19-Jan-05	M291	0.300	-0.523	2	2	O/N, O/N
VR IPA Sol'n	15-Feb-05	M291	0.426	-0.371	2	0	>24
VR IPA Sol'n	17-Feb-05	M291	0.426	-0.371	2	2	O/N, O/N
VR IPA Sol'n	05-Jan-05	M291	0.600	-0.222	1	1	O/N
VR IPA Sol'n	11-Jan-05	M291	0.600	-0.222	1	1	O/N
VR IPA Sol'n	22-Feb-05	M291	0.800	-0.097	2	2	O/N, O/N
VR IPA Sol'n	22-Feb-05	M291	1.00	0.000	1	1	4

Table A3. Raw data for M291 SDK animals challenged with 5% VR IPA solution in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours).

Agent	Date	Treat- ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR Neat	11-Jan-05	RSDL	1.47	0.168	1	0	>24
VR Neat	10-Feb-05	RSDL	6.13	0.788	1	0	>24
VR Neat	05-Jan-05	RSDL	8.00	0.903	1	0	>24
VR Neat	13-Jan-05	RSDL	8.00	0.903	1	0	>24
VR Neat	01-Feb-05	RSDL	8.00	0.903	2	0	>24
VR Neat	25-Jan-05	RSDL	9.24	0.966	2	0	>24
VR Neat	27-Jan-05	RSDL	9.24	0.966	2	1	O/N, >24
VR Neat	11-Jan-05	RSDL	10.7	1.028	1	1	O/N
VR Neat	13-Jan-05	RSDL	10.7	1.028	1	0	>24
VR Neat	19-Jan-05	RSDL	10.7	1.028	2	2	O/N, O/N
VR Neat	01-Feb-05	RSDL	12.0	1.079	1	0	>24
VR Neat	03-Feb-05	RSDL	12.0	1.079	3	0	>24
VR Neat	08-Feb-05	RSDL	13.8	1.140	2	1	O/N, >24
VR Neat	10-Feb-05	RSDL	13.8	1.140	2	2	O/N, O/N
VR Neat	05-Jan-05	RSDL	16.0	1.204	1	1	O/N
VR Neat	10-Feb-05	RSDL	16.0	1.204	1	0	>24
VR Neat	15-Feb-05	RSDL	20.0	1.301	2	1	O/N, >24
VR Neat	15-Feb-05	RSDL	24.0	1.380	2	1	O/N, >24
VR Neat	17-Feb-05	RSDL	24.0	1.380	2	1	O/N, >24
VR Neat	17-Feb-05	RSDL	31.5	1.498	2	1	O/N, >24
VR Neat	24-Feb-05	RSDL	31.5	1.498	2	2	O/N, O/N
VR Neat	22-Feb-05	RSDL	40.0	1.602	2	1	O/N, >24
VR Neat	22-Feb-05	RSDL	50.0	1.699	2	1	O/N, >24
VR Neat	24-Feb-05	RSDL	50.0	1.699	4	3	O/N, O/N, O/N, >24
VR Neat	24-Feb-05	RSDL	75.0	1.875	4	4	2, 2, O/N, O/N
VR Neat	24-Feb-05	RSDL	100	2.000	4	4	2, 2, 3, 3

Table A4. Raw data for RSDL animals challenged with neat VR in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours).

Agent	Date	Treat- ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time of Death
VR IPA Sol'n	27-Jan-05	Soap	1.27	0.104	2	0	>24
VR IPA Sol'n	01-Feb-05	Soap	1.27	0.104	2	0	>24
VR Neat	11-Jan-05	Soap	1.60	0.204	1	0	>24
VR IPA Sol'n	25-Jan-05	Soap	1.60	0.204	1	1	O/N
VR IPA Sol'n	08-Feb-05	Soap	1.60	0.204	2	0	>24
VR Neat	13-Jan-05	Soap	1.94	0.288	2	0	>24
VR Neat	19-Jan-05	Soap	2.14	0.330	2	1	O/N, >24
VR Neat	11-Jan-05	Soap	2.36	0.373	1	1	O/N
VR Neat	25-Jan-05	Soap	2.36	0.373	1	0	>24
VR Neat	05-Jan-05	Soap	3.50	0.544	1	1	O/N
VR Neat	01-Feb-05	Soap	3.50	0.544	1	1	O/N
VR Neat	03-Feb-05	Soap	3.50	0.544	2	0	>24
VR Neat	22-Feb-05	Soap	4.25	0.628	2	2	O/N, O/N
VR Neat	03-Feb-05	Soap	5.00	0.699	1	0	>24
VR Neat	15-Feb-05	Soap	5.00	0.699	2	0	>24
VR Neat	17-Feb-05	Soap	5.00	0.699	2	1	O/N, >24
VR Neat	22-Feb-05	Soap	6.00	0.778	3	3	O/N, O/N, O/N
VR Neat	05-Jan-05	Soap	7.00	0.845	1	1	O/N
VR Neat	08-Feb-05	Soap	7.00	0.845	1	1	O/N
VR Neat	15-Feb-05	Soap	10.0	1.000	2	1	O/N, >24
VR Neat	17-Feb-05	Soap	10.0	1.000	2	2	O/N, O/N
VR Neat	10-Feb-05	Soap	15.0	1.176	2	2	O/N, O/N
VR Neat	15-Feb-05	Soap	20.0	1.301	1	1	O/N
VR Neat	17-Feb-05	Soap	20.0	1.301	1	1	O/N
VR Neat	22-Feb-05	Soap	25.0	1.398	2	2	O/N, O/N

Table A5. Raw data for 1% soapy water animals challenged with neat and 5% VR IPA solution in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours). SAS analysis only used neat animals.

Agent	Date	Treat-ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR Neat	20-Sep-04	Control	0.090	-1.046	4	0	>24
VR Neat	20-Sep-04	Control	0.160	-0.796	4	0	>24
VR Neat	24-Sep-04	Control	0.170	-0.770	4	0	>24
VR Neat	24-Sep-04	Control	0.190	-0.721	4	0	>24
VR Neat	27-Sep-04	Control	0.310	-0.509	4	0	>24
VR Neat	27-Sep-04	Control	0.500	-0.301	3	0	>24
VR Neat	02-Nov-04	Control	0.630	-0.201	4	1	NR, >24, >24, >24
VR Neat	25-Oct-04	Control	0.700	-0.155	4	0	>24
VR Neat	28-Oct-04	Control	0.740	-0.131	4	2	NR, NR, >24, >24
VR Neat	28-Oct-04	Control	0.870	-0.060	4	4	NR, NR, NR, NR
VR Neat	02-Nov-04	Control	0.880	-0.056	4	4	NR, NR, NR, NR
VR Neat	25-Oct-04	Control	0.910	-0.041	4	4	NR, NR, NR, NR

Table A6. Raw data for positive control animals challenged with neat VR in the SERPACWA experiments conducted at Battelle. NR = time of death not recorded.

Agent	Date	Treatment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR Neat	20-Sep-04	SERPACWA	0.090	-1.046	4	0	>24
VR Neat	20-Sep-04	SERPACWA	0.160	-0.796	4	1	NR, >24, >24, >24
VR Neat	24-Sep-04	SERPACWA	0.260	-0.585	4	0	>24
VR Neat	24-Sep-04	SERPACWA	0.390	-0.409	4	0	>24
VR Neat	27-Sep-04	SERPACWA	0.510	-0.292	4	0	>24
VR Neat	27-Sep-04	SERPACWA	0.750	-0.125	4	1	NR, >24, >24, >24
VR Neat	25-Oct-04	SERPACWA	0.870	-0.060	4	1	NR, >24, >24, >24
VR Neat	25-Oct-04	SERPACWA	2.10	0.322	4	0	>24
VR Neat	28-Oct-04	SERPACWA	2.50	0.398	4	3	NR, NR, NR, >24
VR Neat	28-Oct-04	SERPACWA	3.60	0.556	4	2	NR, NR, >24, >24
VR Neat	02-Nov-04	SERPACWA	8.00	0.903	4	4	NR, NR, NR, NR
VR Neat	02-Nov-04	SERPACWA	20.0	1.301	4	4	NR, NR, NR, NR

Table A7. Raw data for SERPACWA animals challenged with neat VR in the SERPACWA experiments conducted at Battelle. NR = time of death not recorded.

Agent	Date	Treatment	Time Delay, min	Number Animals	Number Dead	Time to Death
VR Neat	08-Sep-10	Bleach delayed	2	1	0	>24
VR Neat	08-Sep-10	Bleach delayed	5	2	0	>24
VR Neat	08-Sep-10	Bleach delayed	10	2	0	>24
VR Neat	09-Sep-10	Bleach delayed	10	1	0	>24
VR Neat	31-Aug-10	Bleach delayed	15	1	0	>24
VR Neat	08-Sep-10	Bleach delayed	15	2	1	4, >24
VR Neat	09-Sep-10	Bleach delayed	22	3	1	1, >24, >24
VR Neat	31-Aug-10	Bleach delayed	30	1	1	1
VR Neat	08-Sep-10	Bleach delayed	30	1	0	>24
VR Neat	09-Sep-10	Bleach delayed	30	1	1	O/N
VR Neat	09-Sep-10	Bleach delayed	38	3	3	3, O/N, O/N
VR Neat	31-Aug-10	Bleach delayed	45	1	1	2
VR Neat	09-Sep-10	Bleach delayed	45	1	1	O/N
VR Neat	31-Aug-10	Bleach delayed	60	1	1	2
VR Neat	31-Aug-10	Bleach delayed	75	1	1	2
VR Neat	31-Aug-10	Bleach delayed	90	1	1	2
VR Neat	31-Aug-10	Bleach delayed	105	1	1	2
VR Neat	31-Aug-10	Bleach delayed	120	1	1	2

Table A8. Raw data for delayed decontamination for 0.5% bleach animals challenged with 1.06 mg/kg neat VR (5 LD₅₀s). O/N = overnight (6-20 hours).

Agent	Date	Treatment	Time Delay, min	Number Animals	Number Dead	Time to Death
VR Neat	11-Sep-08	RSDL delayed	5	3	0	>24
VR Neat	11-Sep-08	RSDL delayed	10	1	0	>24
VR Neat	11-Sep-08	RSDL delayed	15	2	0	>24
VR Neat	11-Sep-08	RSDL delayed	30	3	0	>24
VR Neat	18-Sep-08	RSDL delayed	45	4	0	>24
VR Neat	11-Sep-08	RSDL delayed	60	3	1	O/N, >24, >24
VR Neat	18-Sep-08	RSDL delayed	60	1	0	>24
VR Neat	18-Sep-08	RSDL delayed	70	4	3	2, O/N, O/N, >24
VR Neat	18-Sep-08	RSDL delayed	80	4	2	O/N, O/N, >24, >24
VR Neat	11-Sep-08	RSDL delayed	90	3	3	3, O/N, O/N
VR Neat	18-Sep-08	RSDL delayed	120	2	2	2, 2
VR Neat	11-Sep-08	No decon	NA	1	1	3

Table A9. Raw data for delayed decontamination for RSDL animals challenged with 1.06 mg/kg neat VR (5 LD₅₀s), except where noted. NA = not applicable. O/N = overnight (6-20 hours).

Agent	Date	Treatment	Time Delay, min	Number Animals	Number Dead	Time to Death
VR Neat	08-Sep-10	Soap delayed	2	1	0	>24
VR Neat	08-Sep-10	Soap delayed	5	2	0	>24
VR Neat	09-Sep-10	Soap delayed	5	1	0	>24
VR Neat	08-Sep-10	Soap delayed	10	2	0	>24
VR Neat	09-Sep-10	Soap delayed	10	1	0	>24
VR Neat	31-Aug-10	Soap delayed	15	1	1	2
VR Neat	08-Sep-10	Soap delayed	15	2	1	O/N, >24
VR Neat	09-Sep-10	Soap delayed	22	3	1	4, >24, >24
VR Neat	31-Aug-10	Soap delayed	30	1	0	>24
VR Neat	08-Sep-10	Soap delayed	30	1	1	1
VR Neat	09-Sep-10	Soap delayed	30	1	1	O/N
VR Neat	09-Sep-10	Soap delayed	38	3	1	O/N, >24, >24
VR Neat	31-Aug-10	Soap delayed	45	1	1	2
VR Neat	09-Sep-10	Soap delayed	45	1	1	O/N
VR Neat	31-Aug-10	Soap delayed	60	1	1	1
VR Neat	31-Aug-10	Soap delayed	75	1	1	4
VR Neat	31-Aug-10	Soap delayed	90	1	1	2
VR Neat	31-Aug-10	Soap delayed	105	1	1	2
VR Neat	31-Aug-10	Soap delayed	120	1	1	2

Table A10. Raw data for delayed decontamination for 1% soapy water animals challenged with 1.06 mg/kg neat VR (5 LD₅₀s). NA = not applicable. O/N = overnight (6-20 hours).

Agent	Date	Treat- ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR IPA Sol'n	12-Jan-06	Control	0.040	-1.398	2	0	>24
VR IPA Sol'n	10-Jan-06	Control	0.063	-1.201	2	0	>24
VR IPA Sol'n	17-Jan-06	Control	0.090	-1.046	2	0	>24
VR IPA Sol'n	10-Jan-06	Control	0.130	-0.886	2	1	O/N, >24
VR IPA Sol'n	12-Jan-06	Control	0.130	-0.886	2	0	>24
VR IPA Sol'n	17-Jan-06	Control	0.180	-0.745	3	1	O/N, >24, >24
VR IPA Sol'n	10-Jan-06	Control	0.250	-0.602	2	0	>24
VR IPA Sol'n	19-Jan-06	Control	0.250	-0.602	2	1	O/N, >24
VR IPA Sol'n	19-Jan-06	Control	0.300	-0.523	3	3	O/N, O/N, O/N
VR IPA Sol'n	17-Jan-06	Control	0.350	-0.456	3	3	O/N, O/N, O/N
VR IPA Sol'n	12-Jan-06	Control	0.500	-0.301	2	2	O/N, O/N
VR IPA Sol'n	12-Jan-06	Control	0.700	-0.155	2	2	O/N, O/N

Table A11. Raw data for repeat positive control animals challenged with 5% VR IPA solution in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours).

Agent	Date	Treat- ment	Dose mg/kg	Log Dose	Number Animals	Number Dead	Time to Death
VR Neat	19-Jan-06	M291	0.100	-1.000	3	0	>24
VR Neat	19-Jan-06	M291	0.150	-0.824	3	0	>24
VR Neat	10-Jan-06	M291	0.200	-0.699	2	0	>24
VR Neat	17-Jan-06	M291	0.200	-0.699	2	2	O/N, O/N
VR Neat	12-Jan-06	M291	0.250	-0.602	2	1	O/N, >24
VR Neat	17-Jan-06	M291	0.250	-0.602	2	2	O/N, O/N
VR Neat	10-Jan-06	M291	0.316	-0.500	2	1	O/N, >24
VR Neat	17-Jan-06	M291	0.316	-0.500	2	2	O/N, O/N
VR Neat	17-Jan-06	M291	0.400	-0.398	2	2	O/N, O/N
VR Neat	12-Jan-06	M291	0.470	-0.328	2	2	O/N, O/N
VR Neat	12-Jan-06	M291	0.690	-0.161	2	2	3, 4
VR Neat	10-Jan-06	M291	1.00	0.000	2	2	2, 4
VR Neat	12-Jan-06	M291	1.00	0.000	2	2	2, 2
VR Neat	10-Jan-06	M291	3.16	0.500	2	2	2, 2
VR Neat	10-Jan-06	M291	10.0	1.000	2	2	2, 2

Table A12. Raw data for repeat M291 SDK animals challenged with neat VR in the standard 2-minute decontamination product experiments. O/N = overnight (6-20 hours).

APENDIX B: SAS OUTPUT FILES

SAS ANALYSIS USING PROBSEPX AND PRORATIO PROGRAMS FOR DECON VR LD₅₀ Final Report After complete QC Audit of Data on 20 October 2005

File: VR decon SAS output including 95 and 99.5 % CI ehb corrected 150604.doc

LD50 VR

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Acontrol-soln -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD
B1	B01
7.052933	11.020469
	Weighted loss
	16.443866

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD		Method: Gauss-Newton	
Iter	B1	B01	Weighted loss
0	7.052933	11.020469	16.443866
1	8.368452	12.280613	16.068173
2	8.926633	12.783222	16.040642
3	9.023109	12.868112	16.039997
4	9.032368	12.876104	16.039991
5	9.033164	12.876790	16.039991

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD
---	--------------------------

Source	DF	Weighted SS	Weighted MS
Regression	2	1362.7067978	681.3533989
Residual	11	8.4761954	0.7705632
Uncorrected Total	13	1371.1829933	
(Corrected Total)	12	81.6710667	
Sum of Loss		16.0399908	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	9.03316424	4.0480311164	0.1234738031	17.942854687
B01	12.87679010	3.5535572896	5.0554333740	20.698146835

Asymptotic Correlation Matrix

Corr	B1	B01
ffffffffffffffffffffffffffffffff		
B1	1	0.9947710043
B01	0.9947710043	1

LD50 VR

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Bleach-neat -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD	
B1	B01	Weighted loss
2.298077	2.801042	28.440560

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD		Method: Gauss-Newton	
Iter	B1	B01	Weighted loss
0	2.298077	2.801042	28.440560
1	2.993400	2.286399	27.869003
2	3.130920	2.173030	27.854217
3	3.142529	2.164494	27.854085
4	3.143443	2.163850	27.854085
5	3.143520	2.163795	27.854085

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD
---	--------------------------

Source	DF	Weighted SS	Weighted MS
Regression	2	36.107840985	18.053920492
Residual	15	22.171538526	1.478102568
Uncorrected Total	17	58.279379511	
(Corrected Total)	16	43.654667728	
Sum of Loss		27.854084566	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	3.143520242	1.2282031473	0.52567715431	5.7613633301
B01	2.163794568	1.1008251666	-.18254981317	4.5101389487

Asymptotic Correlation Matrix

Corr	B1	B01
ff		
B1	1	-0.968371233
B01	-0.968371233	1

LD50 VR

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Bleach-soln -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD	
B1	B01	Weighted loss
3.142536E-15	3.355146	0.205173

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD		Method: Gauss-Newton	
Iter	B1	B01	Weighted loss
0	3.142536E-15	3.355146	0.205173
1	-5.803366E-16	2.870297	0.066949
2	-3.567413E-15	2.468419	0.022775
3	-2.274981E-15	2.117693	0.007903

4	5.6753318E-16	1.802594	0.002774
5	2.262191E-15	1.514143	0.000981
6	9.9414521E-16	1.246596	0.000349
7	1.2535737E-15	0.996011	0.000125
8	7.8804367E-16	0.759546	0.0000446140
9	1.7418247E-15	0.535073	0.0000160192
10	1.6869728E-15	0.320945	0.0000057640
11	-1.720244E-16	0.115864	0.0000020777
12	-3.78703E-16	-0.081220	0.0000007500
13	-8.114351E-16	-0.271170	0.0000002711
14	-1.68259E-15	-0.454703	0.0000000981
15	-7.418733E-16	-0.632424	0.0000000355
16	-7.326383E-16	-0.804850	0.0000000129
17	5.1420742E-16	-0.972424	4.67508743E-9
18	1.1663402E-15	-1.135531	1.69749992E-9
19	2.8012689E-15	-1.294510	6.1674532E-10
20	-8.3535E-15	-1.449656	2.2420865E-10
21	-6.778937E-15	-1.601233	8.1550322E-11
22	-7.025321E-15	-1.749475	2.9676261E-11
23	4.542982E-15	-1.894591	1.0803802E-11
24	4.6001676E-15	-2.036771	3.9350745E-12
25	6.0572548E-15	-2.176185	1.43352E-12
26	7.2822059E-15	-2.312987	5.22693E-13
27	2.6790135E-15	-2.447319	1.9051427E-13
28	-2.38347E-15	-2.579309	6.9277917E-14
29	5.6712605E-15	-2.709075	2.5313085E-14
30	5.5290026E-15	-2.836725	9.3258734E-15

WARNING: PROC NLIN failed to converge.

Non-Linear Least Squares Summary Statistics Dependent Variable NDEAD

Source	DF	Weighted SS	Weighted MS
Regression	2	-1.069299E-24	-5.346497E-25
Residual	0	1.0692994E-24	0
Uncorrected Total	2	0	
(Corrected Total)	1	0	
Sum of Loss		9.3258734E-15	

WARNING: PROC NLIN failed to converge.

LD50 VR

4

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Bleach-soln -----

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	0.000000000	0	0.0000000000	0.0000000000
B01	-2.836724855	0	-2.8367248550	-2.8367248550

Asymptotic Correlation Matrix

Corr	B1	B01
1		
	1	-0.94999914

1	2.119929	2.301280	53.679678
2	2.130890	2.287966	53.679308
3	2.131443	2.287235	53.679307
4	2.131470	2.287200	53.679307

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable NDEAD

Source	DF	Weighted SS	Weighted MS
Regression	2	163.65337885	81.82668943
Residual	24	21.65314387	0.90221433
Uncorrected Total	26	185.30652272	

(Corrected Total)	25	155.74833488
Sum of Loss		53.67930668

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval
			Lower Upper
B1	2.131469883	0.60607748024	0.88059751602 3.3823422490
B01	2.287199873	0.81480976066	0.60552872258 3.9688710238

Asymptotic Correlation Matrix

Corr	B1	B01
1	1	-0.970000814
B1	-0.970000814	1
B01		

LD50 VR

7

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Soap-neat -----

Non-Linear Least Squares Grid Search Dependent Variable NDEAD

B1	B01	Weighted loss
2.087075	3.972201	32.956058

Non-Linear Least Squares Iterative Phase

Dependent Variable NDEAD	Method: Gauss-Newton
Iter	B1 B01 Weighted loss
0	2.087075 3.972201 32.956058
1	2.492805 3.625188 32.667162
2	2.535358 3.598087 32.665154
3	2.537376 3.596888 32.665149
4	2.537451 3.596843 32.665149

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable NDEAD

Source	DF	Weighted SS	Weighted MS
Regression	2	289.78408628	144.89204314
Residual	18	19.53935002	1.08551945
Uncorrected Total	20	309.32343630	

(Corrected Total) 19 62.62833317
Sum of Loss 32.66514880

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	2.537450772	0.99226817933	0.4527864592	4.6221150854
B01	3.596842900	0.71410138749	2.0965814690	5.0971043306

Asymptotic Correlation Matrix

Corr	B1	B01
1	1	-0.934703419
B1	-0.934703419	1
B01		

LD50 VR

8

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Soap-soln -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD	
	B1	B01
	10.931120	2.220455
		Weighted loss
		4.943808

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD	Method: Gauss-Newton		
Iter	B1	B01	Weighted loss
0	10.931120	2.220455	4.943808
1	14.551747	1.359771	4.632625
2	18.512329	0.546770	4.544230
3	22.008459	-0.166866	4.514488
4	25.149524	-0.808021	4.504230
5	28.024936	-1.394950	4.500644
6	30.691972	-1.939345	4.499379
7	33.189920	-2.449226	4.498930
8	35.547111	-2.930376	4.498770
9	37.784773	-3.387128	4.498713
10	39.919294	-3.822826	4.498693
11	41.963639	-4.240117	4.498685
12	43.928271	-4.641138	4.498683
13	45.821782	-5.027642	4.498682
14	47.651325	-5.401088	4.498681
15	47.651325	-5.401088	4.498681

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics			Dependent Variable NDEAD
Source	DF	Weighted SS	Weighted MS
Regression	1	1.3332563009	1.3332563009
Residual	4	3.9998400104	0.9999600026
Uncorrected Total	5	5.3330963113	
(Corrected Total)	4	5.3329534137	
Sum of Loss		4.4986813534	

NOTE: The (approximate) Hessian is singular.

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	47.65132527	0.00000000000	47.651325265	47.651325265
B01	-5.40108793	0.68140390792	-7.292942874	-3.509232981

Asymptotic Correlation Matrix

Corr	B1	B01
ffffff		
B1	.	.
B01	.	1

LD50 VR

9

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Acontrol-soln -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
1	8	0.080	-1.10	1	0	0.000	-1.64485	-0.08762
2	1	0.100	-1.00	1	0	0.000	-1.64485	-0.15897
3	3	0.100	-1.00	1	0	0.000	-1.64485	-0.15897
4	5	0.120	-.921	2	0	0.000	-1.64485	0.00461
5	7	0.120	-.921	2	2	1.000	1.64485	0.00461
6	2	0.134	-.873	1	1	1.000	1.64485	0.17809
7	3	0.134	-.873	1	0	0.000	-1.64485	0.17809
8	4	0.134	-.873	2	1	0.500	-0.00000	0.35618
9	8	0.164	-.785	2	1	0.500	-0.00000	0.91027
10	6	0.200	-.699	2	2	1.000	1.64485	1.47115
11	2	0.224	-.650	1	1	1.000	1.64485	0.86354
12	7	0.224	-.650	1	1	1.000	1.64485	0.86354
13	1	0.300	-.523	1	1	1.000	1.64485	0.99029

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
1	0.12979	0.02109	-0.15625	0.02109	-1.64485
2	0.40650	0.12376	-0.40814	0.12376	-1.15637
3	0.40650	0.12376	-0.40814	0.12376	-1.15637
4	1.31365	0.65913	-1.10863	0.32956	-0.44112
5	1.31365	0.65913	2.25530	0.32956	-0.44112
6	0.81535	0.49672	1.05160	0.49672	-0.00822
7	0.81535	0.49672	-1.03790	0.49672	-0.00822
8	1.63071	0.99344	0.01016	0.49672	-0.00822
9	2.22406	1.56716	-1.13410	0.78358	0.78435
10	2.29269	1.88192	0.42751	0.94096	1.56288
11	1.09176	0.97765	0.16141	0.97765	1.64485
12	1.09176	0.97765	0.16141	0.97765	1.64485
13	1.00810	0.99919	0.02852	0.99919	1.64485

----- Agent=VR Treatment Group=Bleach-neat -----

Agent Log10

OBS	STAGE	Dose (mg/kg)	Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
14	5	2	0.301	2	0	0.000	-1.64485	-0.15461
15	6	2	0.301	2	0	0.000	-1.64485	-0.15461

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
14	0.27215	0.058770	-0.27100	0.029385	-1.64485
15	0.27215	0.058770	-0.27100	0.029385	-1.64485

LD50 VR

10

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Bleach-neat -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
16	12	3.0	0.477	2	0	0.000	-1.64485	-0.20363
17	1	4.0	0.602	1	1	1.000	1.64485	-0.05976
18	2	4.0	0.602	1	1	1.000	1.64485	-0.05976
19	3	4.0	0.602	1	0	0.000	-1.64485	-0.05976
20	10	5.6	0.748	2	1	0.500	-0.00000	0.15700
21	12	6.5	0.813	2	0	0.000	-1.64485	0.31646
22	1	8.0	0.903	1	0	0.000	-1.64485	0.26467
23	2	8.0	0.903	1	0	0.000	-1.64485	0.26467
24	3	8.0	0.903	1	0	0.000	-1.64485	0.26467
25	9	8.0	0.903	1	0	0.000	-1.64485	0.26467
26	8	9.8	0.991	2	0	0.000	-1.64485	0.70744
27	9	9.8	0.991	2	2	1.000	1.64485	0.70744
28	4	12.0	1.079	2	2	1.000	1.64485	0.87153
29	7	12.0	1.079	2	2	1.000	1.64485	0.87153
30	11	16.0	1.204	2	2	1.000	1.64485	1.11981

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
16	0.56649	0.18143	-0.49872	0.09071	-1.33637
17	0.40513	0.17268	2.28596	0.17268	-0.94362
18	0.40513	0.17268	2.28596	0.17268	-0.94362
19	0.40513	0.17268	-0.47714	0.17268	-0.94362
20	1.09940	0.62820	0.60154	0.31410	-0.48426
21	1.24127	0.77887	-1.18985	0.38943	-0.28080
22	0.73747	0.50107	-1.02772	0.50107	0.00268
23	0.73747	0.50107	-1.02772	0.50107	0.00268
24	0.73747	0.50107	-1.02772	0.50107	0.00268
25	0.73747	0.50107	-1.02772	0.50107	0.00268
26	1.73320	1.22032	-1.88785	0.61016	0.27973
27	1.73320	1.22032	1.20618	0.61016	0.27973
28	1.97235	1.42194	0.98514	0.71097	0.55622
29	1.97235	1.42194	0.98514	0.71097	0.55622
30	2.19492	1.65736	0.72994	0.82868	0.94897

LD50 VR

11

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
 OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Bleach-soln -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile
31	8	1.26	0.100	1	0	0.000	-1.64485
32	7	1.58	0.199	1	0	0.000	-1.64485

OBS	LCL	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
31	.	.	2.3122E-15	.	2.3122E-15	-1.64485
32	.	.	2.3122E-15	.	2.3122E-15	-1.64485

----- Agent=VR Treatment Group=M291-soln -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
33	8	0.080	-1.10	1	0	0.000	-1.64485	-0.12703
34	8	0.100	-1.00	2	0	0.000	-1.64485	-0.17852
35	7	0.150	-.824	1	1	1.000	1.64485	0.08240
36	11	0.150	-.824	2	0	0.000	-1.64485	0.16480
37	7	0.175	-.757	2	2	1.000	1.64485	0.34626
38	9	0.175	-.757	2	0	0.000	-1.64485	0.34626
39	6	0.200	-.699	2	1	0.500	-0.00000	0.50717
40	10	0.200	-.699	2	2	1.000	1.64485	0.50717
41	3	0.260	-.585	2	0	0.000	-1.64485	0.78635
42	5	0.260	-.585	2	2	1.000	1.64485	0.78635
43	1	0.300	-.523	1	0	0.000	-1.64485	0.45384
44	2	0.300	-.523	1	1	1.000	1.64485	0.45384
45	4	0.300	-.523	2	2	1.000	1.64485	0.90767

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
33	0.37345	0.12321	-0.40193	0.12321	-1.15907
34	0.92231	0.37189	-0.76766	0.18595	-0.89293
35	0.59989	0.34115	1.43864	0.34115	-0.40934
36	1.19979	0.68229	-1.09341	0.34115	-0.40934
37	1.29695	0.82160	1.79011	0.41080	-0.22548
38	1.29695	0.82160	-1.24810	0.41080	-0.22548
39	1.38724	0.94720	0.07826	0.47360	-0.06622
40	1.38724	0.94720	1.56057	0.47360	-0.06622
41	1.60336	1.19486	-1.79412	0.59743	0.24670
42	1.60336	1.19486	1.20895	0.59743	0.24670
43	0.86976	0.66180	-1.43021	0.66180	0.41737
44	0.86976	0.66180	0.73089	0.66180	0.41737
45	1.73952	1.32359	1.05793	0.66180	0.41737

LD50 VR

12

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
 OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=M291-soln -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
46	11	0.426	-.371	2	0	0.000	-1.64485	1.15671
47	12	0.426	-.371	2	2	1.000	1.64485	1.15671
48	1	0.600	-.222	1	1	1.000	1.64485	0.69718
49	2	0.600	-.222	1	1	1.000	1.64485	0.69718
50	13	0.800	-.097	2	2	1.000	1.64485	1.58697
51	13	1.000	0.000	1	1	1.000	1.64485	0.85793

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
46	2.03653	1.59662	-3.02513	0.79831	0.83560
47	2.03653	1.59662	0.76429	0.79831	0.83560
48	1.08935	0.89327	0.36246	0.89327	1.24408
49	1.08935	0.89327	0.36246	0.89327	1.24408
50	2.18810	1.88753	0.38383	0.94377	1.58720
51	1.07823	0.96808	0.19012	0.96808	1.64485

----- Agent=VR Treatment Group=RSDL-neat -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
52	2	1.472	0.168	1	0	0.000	-1.64485	-0.02760
53	10	6.130	0.787	1	0	0.000	-1.64485	-0.02817
54	1	8.000	0.903	1	0	0.000	-1.64485	0.02614
55	3	8.000	0.903	1	0	0.000	-1.64485	0.02614
56	7	8.000	0.903	2	0	0.000	-1.64485	0.05227
57	5	9.240	0.966	2	0	0.000	-1.64485	0.13382
58	6	9.240	0.966	2	1	0.500	-0.00000	0.13382
59	2	10.670	1.028	1	1	1.000	1.64485	0.11478
60	3	10.670	1.028	1	0	0.000	-1.64485	0.11478

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
52	0.04613	0.00926	-0.09837	0.00926	-1.64485
53	0.32914	0.15049	-0.43377	0.15049	-1.03435
54	0.40462	0.21538	-0.53745	0.21538	-0.78789
55	0.40462	0.21538	-0.53745	0.21538	-0.78789
56	0.80925	0.43076	-0.78080	0.21538	-0.78789
57	0.89176	0.51279	-0.86975	0.25640	-0.65450
58	0.89176	0.51279	0.82636	0.25640	-0.65450
59	0.48738	0.30108	1.55395	0.30108	-0.52130
60	0.48738	0.30108	-0.66941	0.30108	-0.52130

LD50 VR

13

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=RSDL-neat -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
61	4	10.67	1.028	2	2	1.000	1.64485	0.22955
62	7	12.00	1.079	1	0	0.000	-1.64485	0.15816
63	8	12.00	1.079	3	0	0.000	-1.64485	0.47448
64	9	13.80	1.140	2	1	0.500	-0.00000	0.42638
65	10	13.80	1.140	2	2	1.000	1.64485	0.42638
66	1	16.00	1.204	1	1	1.000	1.64485	0.27314
67	10	16.00	1.204	1	0	0.000	-1.64485	0.27314
68	11	20.00	1.301	2	1	0.500	-0.00000	0.72251
69	11	24.00	1.380	2	1	0.500	-0.00000	0.85497
70	12	24.00	1.380	2	1	0.500	-0.00000	0.85497
71	12	31.50	1.498	2	1	0.500	-0.00000	1.03135
72	14	31.50	1.498	2	2	1.000	1.64485	1.03135
73	13	40.00	1.602	2	1	0.500	-0.00000	1.17229
74	13	50.00	1.699	2	1	0.500	-0.00000	1.29781
75	14	50.00	1.699	4	3	0.750	0.67449	2.59561
76	14	75.00	1.875	4	4	1.000	1.64485	3.02563
77	14	100.00	2.000	4	4	1.000	1.64485	3.29626

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
61	0.97477	0.60216	2.24330	0.30108	-0.52130
62	0.52177	0.33997	-0.73041	0.33997	-0.41256
63	1.56531	1.01990	-1.31303	0.33997	-0.41256
64	1.12769	0.77704	0.33375	0.38852	-0.28318
65	1.12769	0.77704	1.83065	0.38852	-0.28318
66	0.61058	0.44186	1.13942	0.44186	-0.14625
67	0.61058	0.44186	-0.90204	0.44186	-0.14625
68	1.37367	1.04809	-0.06985	0.52404	0.06031
69	1.50741	1.18119	-0.26756	0.59060	0.22908
70	1.50741	1.18119	-0.26756	0.59060	0.22908
71	1.70734	1.36934	-0.58038	0.68467	0.48080
72	1.70734	1.36934	0.99100	0.68467	0.48080
73	1.86228	1.51728	-0.88939	0.75864	0.70194
74	1.97497	1.63639	-1.22336	0.81819	0.90850
75	3.94994	3.27278	-0.39073	0.81819	0.90850
76	4.17757	3.60160	0.75176	0.90040	1.28384
77	4.21931	3.75778	0.57483	0.93945	1.55014

LD50 VR

14

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Soap-neat -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
78	3	1.94	0.288	2	0	0.000	-1.64485	-0.11185
79	4	2.14	0.330	2	1	0.500	-0.00000	-0.03364
80	2	2.36	0.373	1	1	1.000	1.64485	0.02865
81	5	2.36	0.373	1	0	0.000	-1.64485	0.02865

82	1	3.50	0.544	1	1	1.000	1.64485	0.25296
83	7	3.50	0.544	1	1	1.000	1.64485	0.25296
84	8	3.50	0.544	2	0	0.000	-1.64485	0.50592
85	13	4.25	0.628	2	2	1.000	1.64485	0.72783
86	8	5.00	0.699	1	0	0.000	-1.64485	0.44482
87	11	5.00	0.699	2	0	0.000	-1.64485	0.88965
88	12	5.00	0.699	2	1	0.500	-0.00000	0.88965
89	13	6.00	0.778	3	3	1.000	1.64485	1.56207
90	1	7.00	0.845	1	1	1.000	1.64485	0.57582
91	9	7.00	0.845	1	1	1.000	1.64485	0.57582
92	11	10.00	1.000	2	1	0.500	-0.00000	1.38023
93	12	10.00	1.000	2	2	1.000	1.64485	1.38023
94	10	15.00	1.176	2	2	1.000	1.64485	1.61707
95	11	20.00	1.301	1	1	1.000	1.64485	0.87804
96	12	20.00	1.301	1	1	1.000	1.64485	0.87804
97	13	25.00	1.398	2	2	1.000	1.64485	1.83954

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
78	1.11390	0.50103	-0.92970	0.25051	-0.67287
79	1.17813	0.57224	0.74992	0.28612	-0.56475
80	0.61908	0.32387	1.51475	0.32387	-0.45691
81	0.61908	0.32387	-0.72556	0.32387	-0.45691
82	0.72900	0.49098	1.04538	0.49098	-0.02261
83	0.72900	0.49098	1.04538	0.49098	-0.02261
84	1.45800	0.98196	-1.46626	0.49098	-0.02261
85	1.57566	1.15175	1.26763	0.57587	0.19135
86	0.84412	0.64447	-1.37369	0.64447	0.37044
87	1.68825	1.28895	-1.98384	0.64447	0.37044
88	1.68825	1.28895	-0.44473	0.64447	0.37044
89	2.73467	2.14837	1.16760	0.71612	0.57136
90	0.96563	0.77073	0.55919	0.77073	0.74124
91	0.96563	0.77073	0.55919	0.77073	0.74124
92	2.10643	1.74333	-1.68820	0.87166	1.13429
93	2.10643	1.74333	0.58294	0.87166	1.13429
94	2.15523	1.88615	0.37746	0.94307	1.58112
95	1.06428	0.97116	0.17867	0.97116	1.64485
96	1.06428	0.97116	0.17867	0.97116	1.64485
97	2.09640	1.96797	0.19214	0.98399	1.64485

LD50 VR

15

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Soap-soln -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
98	6	1.27	0.104	2	0	0.000	-1.64485	-0.00000
99	7	1.27	0.104	2	0	0.000	-1.64485	-0.00000
100	2	1.60	0.204	1	0	0.000	-1.64485	-0.35113
101	5	1.60	0.204	1	1	1.000	1.64485	-0.35113
102	9	1.60	0.204	2	0	0.000	-1.64485	-0.70226

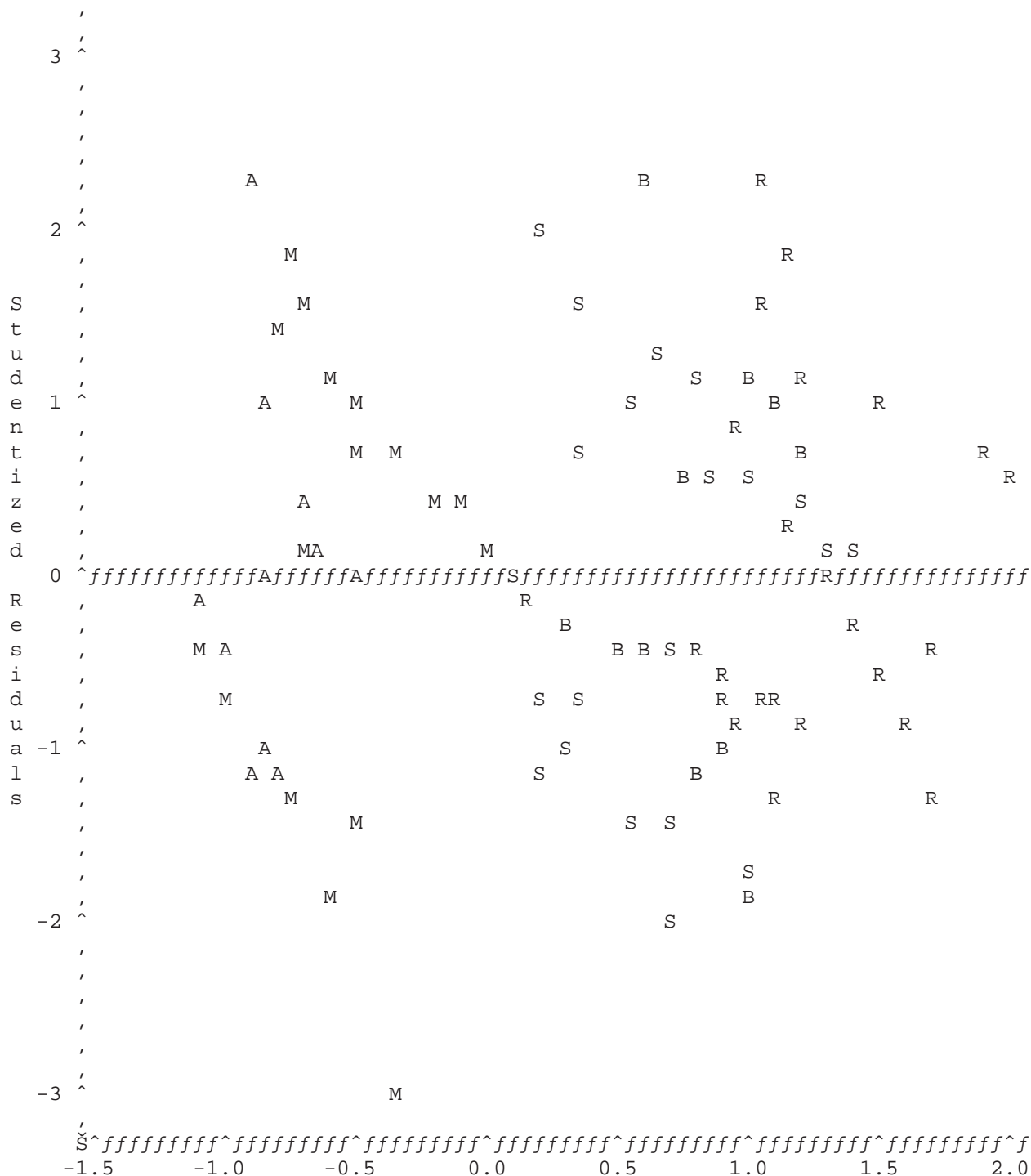
OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
-----	-----	-----------------------	--------------------------	-------------------------	--------------------------

98	0.00000	0.00000	-0.00002	0.00000	-1.64485
99	0.00000	0.00000	-0.00002	0.00000	-1.64485
100	0.85112	0.25000	-0.66664	0.25000	-0.67450
101	0.85112	0.25000	1.99996	0.25000	-0.67450
102	1.70225	0.49999	-1.15468	0.25000	-0.67450

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

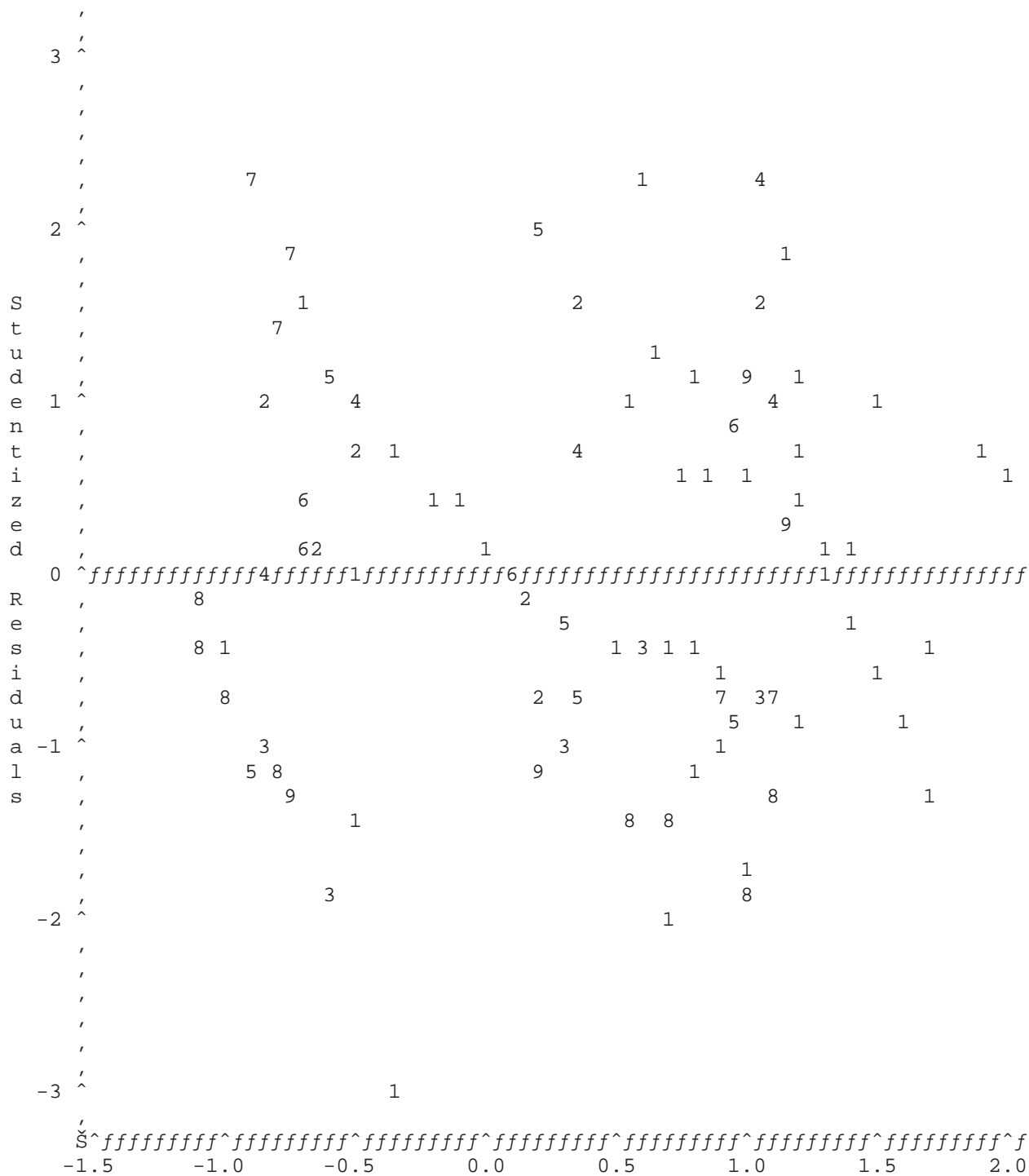
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS TREATMENT GROUP



11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS EXPERIMENTAL STAGE



11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=1 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.2017417	10	1.1161328	0.3529522	-1.4302117	2.2859640

----- Agent=VR Experimental Stage=2 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.5868301	10	1.0434433	0.3299657	-1.0277200	2.2859640

----- Agent=VR Experimental Stage=3 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.8601987	8	0.4517180	0.1597064	-1.7941219	-0.4081377

----- Agent=VR Experimental Stage=4 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
1.0092902	5	0.8048676	0.3599477	0.0101612	2.2432954

----- Agent=VR Experimental Stage=5 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.0389943	6	1.2678872	0.5176128	-1.1086302	1.9999600

----- Agent=VR Experimental Stage=6 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.2122259	5	0.4242678	0.1897383	-0.2709972	0.8263649

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=7 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.6849729	9	1.0822648	0.3607549	-0.7808002	2.2552980

----- Agent=VR Experimental Stage=8 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-1.0625982	8	0.5798417	0.2050050	-1.8878521	-0.1562546

----- Agent=VR Experimental Stage=9 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.2218973	6	1.0517396	0.4293709	-1.2481019	1.2061803

----- Agent=VR Experimental Stage=10 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.5057355	6	1.0731476	0.4381107	-0.9020429	1.8306516

----- Agent=VR Experimental Stage=11 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.9024228	8	1.2682300	0.4483870	-3.0251262	0.7299370

----- Agent=VR Experimental Stage=12 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.1819162	8	0.6504712	0.2299763	-1.1898453	0.7642906

LD50 VR 20

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=13 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.1555078	7	0.9406479	0.3555315	-1.2233630	1.2676264

----- Agent=VR Experimental Stage=14 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.4817159	4	0.6061148	0.3030574	-0.3907283	0.9910012

LD50 VR 21

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure Class Level Information

Class	Levels	Values
STAGE	14	1 2 3 4 5 6 7 8 9 10 11 12 13 14

Number of observations in by group = 102

NOTE: Due to missing values, only 100 observations can be used in this analysis.

LD50 VR 22

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure

Dependent Variable: STUDRES		Studentized Residuals			
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	14	38.05362388	2.71811599	2.98	0.0010
Error	85	77.42858620	0.91092454		
Corrected Total	99	115.48221008			
	R-Square	C.V.	Root MSE	STUDRES Mean	
	0.329519	9060.584	0.954424	0.010534	

Source	DF	Type I SS	Mean Square	F Value	Pr > F
STAGE	13	38.04960098	2.92689238	3.21	0.0006
LOGDOSE	1	0.00402290	0.00402290	0.00	0.9472

Source	DF	Type III SS	Mean Square	F Value	Pr > F
STAGE	13	38.04503287	2.92654099	3.21	0.0006
LOGDOSE	1	0.00402290	0.00402290	0.00	0.9472

LD50 VR

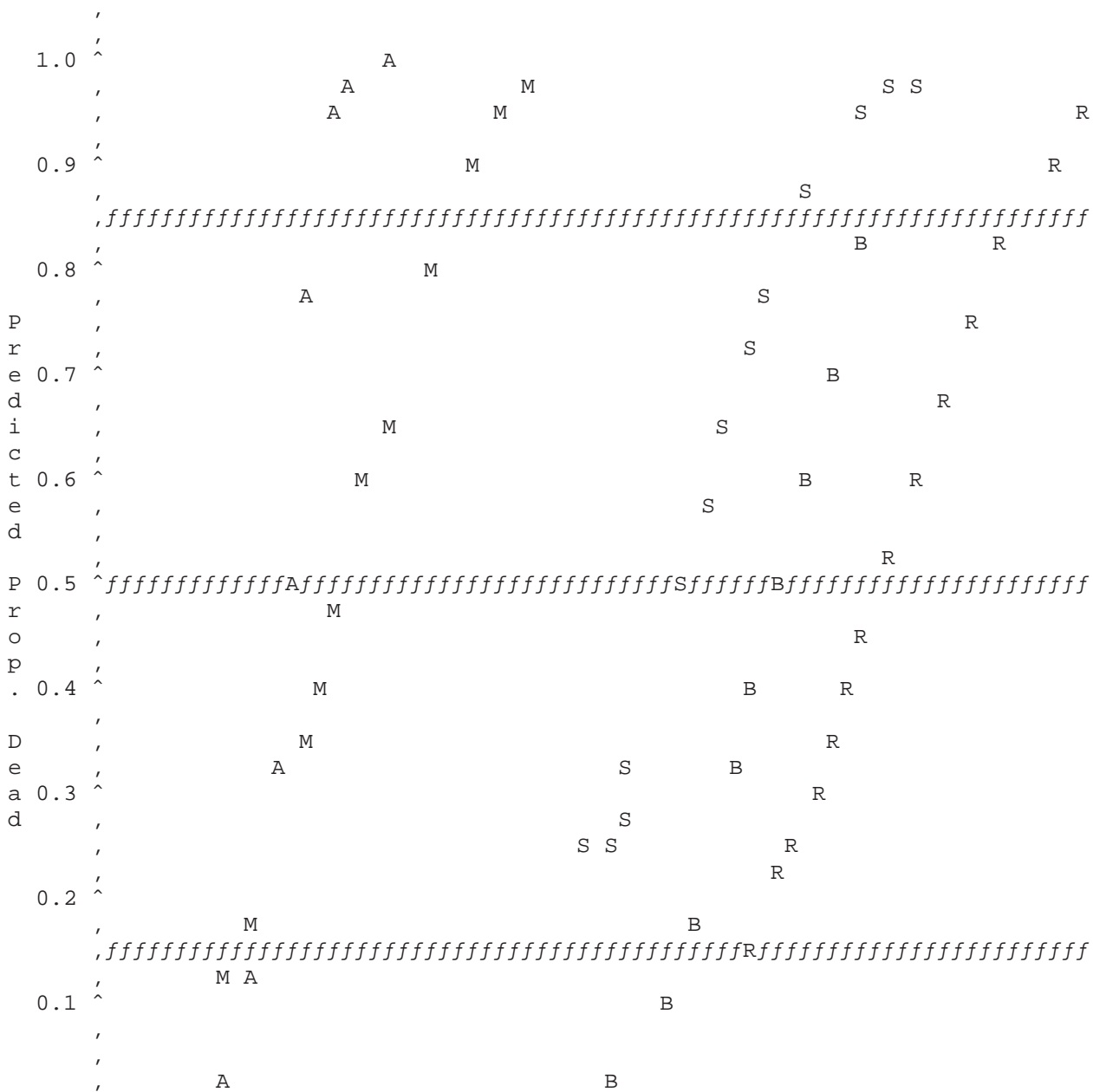
23

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBABILITY PLOT OF PREDICTED PERCENT DEAD WITH 16%, 50%, 84% REFERENCE LINES

----- Agent=VR -----



----- Agent=VR Treatment Group=Bleach-neat -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	0.16219	0.28926
VR	10	-1.28155	0.49456	0.17005
VR	16	-0.99446	0.58589	0.14064
VR	30	-0.52440	0.73542	0.10157
VR	50	-0.00000	0.90224	0.08840
VR	70	0.52440	1.06906	0.11751
VR	84	0.99446	1.21859	0.16249
VR	90	1.28155	1.30992	0.19353

Effective Dose for Percentile	Lower Confid-ence Bound	Upper Confid-ence Bound
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1.4528	0.0067	3.127
3.1229	0.1676	5.082
3.8538	0.3978	5.918
5.4377	1.5324	8.121
7.9843	4.7544	16.774
11.7235	7.8780	64.874
16.5421	10.3283	261.574
20.4136	11.9125	627.027

LD50 VR

26

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=Bleach-neat -----
(continued)

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	99	2.32635	1.64228	0.31491

Effective Dose for Percentile	Lower Confid-ence Bound	Upper Confid-ence Bound
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43.8818	19.1401	15800.20
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----- Agent=VR Treatment Group=Bleach-soln -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	.	.
VR	10	-1.28155	.	.
VR	16	-0.99446	.	.
VR	30	-0.52440	.	.
VR	50	-0.00000	.	.
VR	70	0.52440	.	.
VR	84	0.99446	.	.
VR	90	1.28155	.	.
VR	99	2.32635	.	.

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
.	.	.
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.	.	.

----- Agent=VR Treatment Group=M291-soln -----

Agent	Perc- entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-1.52195	0.37401

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
0.030064	.000012076	0.078973

LD50 VR

27

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=M291-soln -----
(continued)

Agent	Perc- entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	10	-1.28155	-1.14151	0.22833
VR	16	-0.99446	-1.03697	0.19037
VR	30	-0.52440	-0.86581	0.13368
VR	50	-0.00000	-0.67486	0.09263
VR	70	0.52440	-0.48391	0.10542
VR	84	0.99446	-0.31274	0.15307
VR	90	1.28155	-0.20820	0.18875
VR	99	2.32635	0.17224	0.33154

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
0.07219	0.00074	0.13
0.09184	0.00228	0.16
0.13620	0.01382	0.21
0.21142	0.08435	0.35
0.32817	0.21699	1.40
0.48669	0.30933	7.93
0.61915	0.36598	24.02
1.48675	0.62804	1455.19

----- Agent=VR Treatment Group=RSDL-neat -----

Perc-	Probit of	Log(Eff. Dose)	Std. Error of
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Agent	entile	Percentile	for Percentile	Log(Eff. Dose)
VR	1	-2.32635	0.18131	0.33250
VR	10	-1.28155	0.67148	0.20246
VR	16	-0.99446	0.80618	0.16935
VR	30	-0.52440	1.02671	0.12189
VR	50	-0.00000	1.27274	0.09336
VR	70	0.52440	1.51876	0.11119
VR	84	0.99446	1.73930	0.15476
VR	90	1.28155	1.87399	0.18681
VR	99	2.32635	2.36417	0.31544

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
1.518	0.0552	4.07
4.693	0.6761	8.77
6.400	1.3288	10.97
10.634	3.8731	16.42
18.739	10.9091	30.16
33.019	21.6652	78.56
54.865	33.1706	223.88
74.815	41.7320	437.59
231.295	90.6055	5326.35

LD50 VR

28

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=Soap-neat -----

Agent	Perc- entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-0.36383	0.41748
VR	10	-1.28155	0.04792	0.26399
VR	16	-0.99446	0.16107	0.22368
VR	30	-0.52440	0.34631	0.16215
VR	50	-0.00000	0.55298	0.11044
VR	70	0.52440	0.75964	0.10565
VR	84	0.99446	0.94489	0.14607
VR	90	1.28155	1.05803	0.18087
VR	99	2.32635	1.46978	0.32737

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
0.4327	0.0002	1.29
1.1167	0.0091	2.28
1.4490	0.0272	2.70
2.2198	0.1595	3.63
3.5726	1.0113	5.76
5.7497	3.4524	16.94
8.8083	5.5183	83.80
11.4297	6.7372	242.71
29.4974	12.3821	13089.26

----- Agent=VR Treatment Group=Soap-soln -----

Perc- Probit of Log(Eff. Dose) Std. Error of

Agent	entile	Percentile	for Percentile	Log(Eff. Dose)
VR	1	-2.32635	0.16945	.
VR	10	-1.28155	0.19138	.
VR	16	-0.99446	0.19741	.
VR	30	-0.52440	0.20727	.
VR	50	-0.00000	0.21827	.
VR	70	0.52440	0.22928	.
VR	84	0.99446	0.23914	.
VR	90	1.28155	0.24517	.

Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound
1.47725	1.38493	1.57573
1.55375	1.45664	1.65733
1.57545	1.47699	1.68048
1.61165	1.51092	1.71909
1.65301	1.54970	1.76320
1.69543	1.58947	1.80845
1.73438	1.62599	1.85000
1.75861	1.64870	1.87584

LD50 VR

29

11:37 Thursday, October 20, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=Soap-soln -----
(continued)

Agent	Perc- entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	99	2.32635	0.26710	.
Effective Dose for Percentile	Lower Confid- ence Bound	Upper Confid- ence Bound		
1.84967	1.73407	1.97298		

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
 PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
 RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----

Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
Acontrol-soln	-0.87199	0.04018	-0.95074	-0.79323	0.1343	0.1120	0.1610
Bleach-neat	0.90224	0.08840	0.72898	1.07550	7.9843	5.3577	11.8987
Bleach-soln
M291-soln	-0.67486	0.09263	-0.85642	-0.49330	0.2114	0.1392	0.3211
RSDL-neat	1.27274	0.09336	1.08976	1.45572	18.7386	12.2958	28.5574
Soap-neat	0.55298	0.11044	0.33652	0.76943	3.5726	2.1703	5.8808
Soap-soln	0.21827	.	.	.	1.6530	.	.

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----										
1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confid- ence Bound	Upper Confid- ence Bound		
Acontrol-soln	Bleach-neat	-0.87199	0.90224	1.77422	0.09710	59.460	38.3623	92.160		
Acontrol-soln	Bleach-soln	-0.87199		
Acontrol-soln	M291-soln	-0.87199	-0.67486	0.19713	0.10097	1.574	0.9982	2.483		
Acontrol-soln	RSDL-neat	-0.87199	1.27274	2.14472	0.10164	139.548	88.2089	220.766		
Acontrol-soln	Soap-neat	-0.87199	0.55298	1.42496	0.11752	26.605	15.6541	45.217		
Acontrol-soln	Soap-soln	-0.87199	0.21827	1.09026	.	12.310	.	.		
Bleach-neat	Bleach-soln	0.90224		
Bleach-neat	M291-soln	0.90224	-0.67486	-1.57710	0.12804	0.026	0.0149	0.047		
Bleach-neat	RSDL-neat	0.90224	1.27274	0.37050	0.12857	2.347	1.3137	4.193		
Bleach-neat	Soap-neat	0.90224	0.55298	-0.34926	0.14146	0.447	0.2363	0.847		
Bleach-neat	Soap-soln	0.90224	0.21827	-0.68396	.	0.207	.	.		
Bleach-soln	M291-soln	.	-0.67486		
Bleach-soln	RSDL-neat	.	1.27274		
Bleach-soln	Soap-neat	.	0.55298		
Bleach-soln	Soap-soln	.	0.21827		
M291-soln	RSDL-neat	-0.67486	1.27274	1.94759	0.13152	88.633	48.9578	160.459		
M291-soln	Soap-neat	-0.67486	0.55298	1.22784	0.14414	16.898	8.8169	32.386		
M291-soln	Soap-soln	-0.67486	0.21827	0.89313	.	7.819	.	.		
RSDL-neat	Soap-neat	1.27274	0.55298	-0.71976	0.14461	0.191	0.0993	0.366		
RSDL-neat	Soap-soln	1.27274	0.21827	-1.05446	.	0.088	.	.		
Soap-neat	Soap-soln	0.55298	0.21827	-0.33470	.	0.463	.	.		

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
 PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
 RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----									
Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound		
Acontrol-soln	-0.87199	0.04018	-0.98502	-0.75896	0.1343	0.1035	0.1742		
Bleach-neat	0.90224	0.08840	0.65357	1.15090	7.9843	4.5037	14.1548		
Bleach-soln		
M291-soln	-0.67486	0.09263	-0.93543	-0.41428	0.2114	0.1160	0.3852		
RSDL-neat	1.27274	0.09336	1.01012	1.53535	18.7386	10.2358	34.3046		
Soap-neat	0.55298	0.11044	0.24232	0.86364	3.5726	1.7471	7.3053		
Soap-soln	0.21827	.	.	.	1.6530	.	.		

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----										
1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confid- ence Bound	Upper Confid- ence Bound		
Acontrol-soln	Bleach-neat	-0.87199	0.90224	1.77422	0.09710	59.460	31.7012	111.525		
Acontrol-soln	Bleach-soln	-0.87199		
Acontrol-soln	M291-soln	-0.87199	-0.67486	0.19713	0.10097	1.574	0.8186	3.028		
Acontrol-soln	RSDL-neat	-0.87199	1.27274	2.14472	0.10164	139.548	72.2463	269.544		
Acontrol-soln	Soap-neat	-0.87199	0.55298	1.42496	0.11752	26.605	12.4275	56.957		
Acontrol-soln	Soap-soln	-0.87199	0.21827	1.09026	.	12.310	.	.		
Bleach-neat	Bleach-soln	0.90224		
Bleach-neat	M291-soln	0.90224	-0.67486	-1.57710	0.12804	0.026	0.0116	0.061		
Bleach-neat	RSDL-neat	0.90224	1.27274	0.37050	0.12857	2.347	1.0205	5.397		
Bleach-neat	Soap-neat	0.90224	0.55298	-0.34926	0.14146	0.447	0.1790	1.119		
Bleach-neat	Soap-soln	0.90224	0.21827	-0.68396	.	0.207	.	.		
Bleach-soln	M291-soln	.	-0.67486		
Bleach-soln	RSDL-neat	.	1.27274		
Bleach-soln	Soap-neat	.	0.55298		
Bleach-soln	Soap-soln	.	0.21827		
M291-soln	RSDL-neat	-0.67486	1.27274	1.94759	0.13152	88.633	37.8128	207.754		
M291-soln	Soap-neat	-0.67486	0.55298	1.22784	0.14414	16.898	6.6430	42.984		
M291-soln	Soap-soln	-0.67486	0.21827	0.89313	.	7.819	.	.		
RSDL-neat	Soap-neat	1.27274	0.55298	-0.71976	0.14461	0.191	0.0747	0.486		
RSDL-neat	Soap-soln	1.27274	0.21827	-1.05446	.	0.088	.	.		
Soap-neat	Soap-soln	0.55298	0.21827	-0.33470	.	0.463	.	.		

SAS ANALYSIS USING PROBSEPX AND PRORATIO PROGRAMS FOR M291 SDK Repeat DECON VR LD₅₀
Final Report After complete QC Audit of Data on 1 February 2006

File: VR M291 Repeat SAS output including 95 and 99.5 % CI final b 060201 ehb corrected 150604.doc

LD50 VR 1

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=AControl -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD		
B1	B01	Weighted loss	
3.294208	7.242804	19.985104	

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD Method: Gauss-Newton			
Iter	B1	B01	Weighted loss
0	3.294208	7.242804	19.985104
1	4.535052	8.065288	18.574486
2	5.284340	8.555936	18.316588
3	5.490988	8.696716	18.303044
4	5.509174	8.711081	18.302886
5	5.510730	8.712305	18.302885
6	5.510855	8.712404	18.302885

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD
---	--------------------------

Source	DF	Weighted SS	Weighted MS
Regression	2	1090.4232177	545.2116088
Residual	10	8.2047616	0.8204762
Uncorrected Total	12	1098.6279793	
(Corrected Total)	11	1077.0535163	
Sum of Loss		18.3028850	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval Lower Upper
B1	5.510854554	1.9563694473	1.1517643633 9.869944745
B01	8.712403627	1.3201518245	5.7709035560 11.653903698

Asymptotic Correlation Matrix

Corr	B1	B01
B1	1	0.9671630393
B01	0.9671630393	1

LD50 VR 2

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=M291 -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD
--------------------------------------	--------------------------

B1	B01	Weighted loss
1.518704	6.254991	26.032126

Non-Linear Least Squares Iterative Phase

Dependent Variable	NDEAD	Method:	Gauss-Newton
Iter	B1	B01	Weighted loss
0	1.518704	6.254991	26.032126
1	3.167972	7.118441	20.121171
2	4.860195	8.206624	17.424364
3	6.400685	9.217514	16.461818
4	7.305273	9.798271	16.294464
5	7.550681	9.949872	16.285742
6	7.576167	9.964437	16.285632
7	7.578193	9.965568	16.285631
8	7.578356	9.965659	16.285631

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable NDEAD

Source	DF	Weighted SS	Weighted MS
Regression	2	1570120.0604	785060.0302
Residual	13	9.2586	0.7122
Uncorrected Total	15	1570129.3190	
(Corrected Total)	14	328.1612	
Sum of Loss		16.2856	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	7.578356409	2.9026756989	1.3075105642	13.849202255
B01	9.965659486	1.8805825388	5.9029103459	14.028408627

Asymptotic Correlation Matrix

Corr	B1	B01
1	1	0.9819381045
B1	0.9819381045	1
B01		

LD50 VR

3

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES ANDRESIDUALS

----- Agent=VR Treatment Group=AControl -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
1	2	0.040	-1.40	2	0	0.000	-1.64485	-0.00086
2	1	0.063	-1.20	2	0	0.000	-1.64485	-0.02575
3	3	0.090	-1.05	2	0	0.000	-1.64485	-0.14189
4	1	0.130	-.886	2	1	0.500	-0.00000	-0.26595
5	2	0.130	-.886	2	0	0.000	-1.64485	-0.26595
6	3	0.180	-.745	3	1	0.333	-0.43073	0.10246
7	1	0.250	-.602	2	0	0.000	-1.64485	0.73155
8	4	0.250	-.602	2	1	0.500	-0.00000	0.73155

9	4	0.300	-.523	3	3	1.000	1.64485	1.59658
10	3	0.350	-.456	3	3	1.000	1.64485	1.99191
11	2	0.500	-.301	2	2	1.000	1.64485	1.79476
12	2	0.700	-.155	2	2	1.000	1.64485	1.96499

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
1	0.00099	0.00007	-0.00756	0.00003	-1.64485
2	0.03311	0.00368	-0.06214	0.00184	-1.64485
3	0.22250	0.04030	-0.22249	0.02015	-1.64485
4	0.74953	0.24179	1.89174	0.12089	-1.17053
5	0.74953	0.24179	-0.60327	0.12089	-1.17053
6	1.98342	1.04294	-0.06059	0.34765	-0.39168
7	1.88208	1.30682	-2.10262	0.65341	0.39454
8	1.88208	1.30682	-0.49366	0.65341	0.39454
9	3.18532	2.39095	1.01748	0.79698	0.83089
10	3.31748	2.65469	0.74112	0.88490	1.19983
11	2.12518	1.95997	0.21792	0.97999	1.64485
12	2.02651	1.99575	0.06672	0.99787	1.64485

----- Agent=VR Treatment Group=M291 -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
13	4	0.10	-1.00	3	0	0.000	-1.64485	-0.08142
14	4	0.15	-.824	3	0	0.000	-1.64485	-0.44157
15	1	0.20	-.699	2	0	0.000	-1.64485	0.08813

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
13	0.10837	0.01347	-0.12568	0.00449	-1.64485
14	1.04509	0.30176	-0.77139	0.10059	-1.27821
15	1.39258	0.74035	-1.20874	0.37018	-0.33138

LD50 VR

4

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES ANDRESIDUALS

----- Agent=VR Treatment Group=M291 -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
16	3	0.200	-.699	2	2	1.000	1.64485	0.08813
17	2	0.250	-.602	2	1	0.500	-0.00000	0.72617
18	3	0.250	-.602	2	2	1.000	1.64485	0.72617
19	1	0.316	-.500	2	1	0.500	-0.00000	1.30013
20	3	0.316	-.500	2	2	1.000	1.64485	1.30013
21	3	0.400	-.398	2	2	1.000	1.64485	1.74856
22	2	0.470	-.328	2	2	1.000	1.64485	1.91037
23	2	0.690	-.161	2	2	1.000	1.64485	1.99760
24	1	1.000	0.000	2	2	1.000	1.64485	1.99998

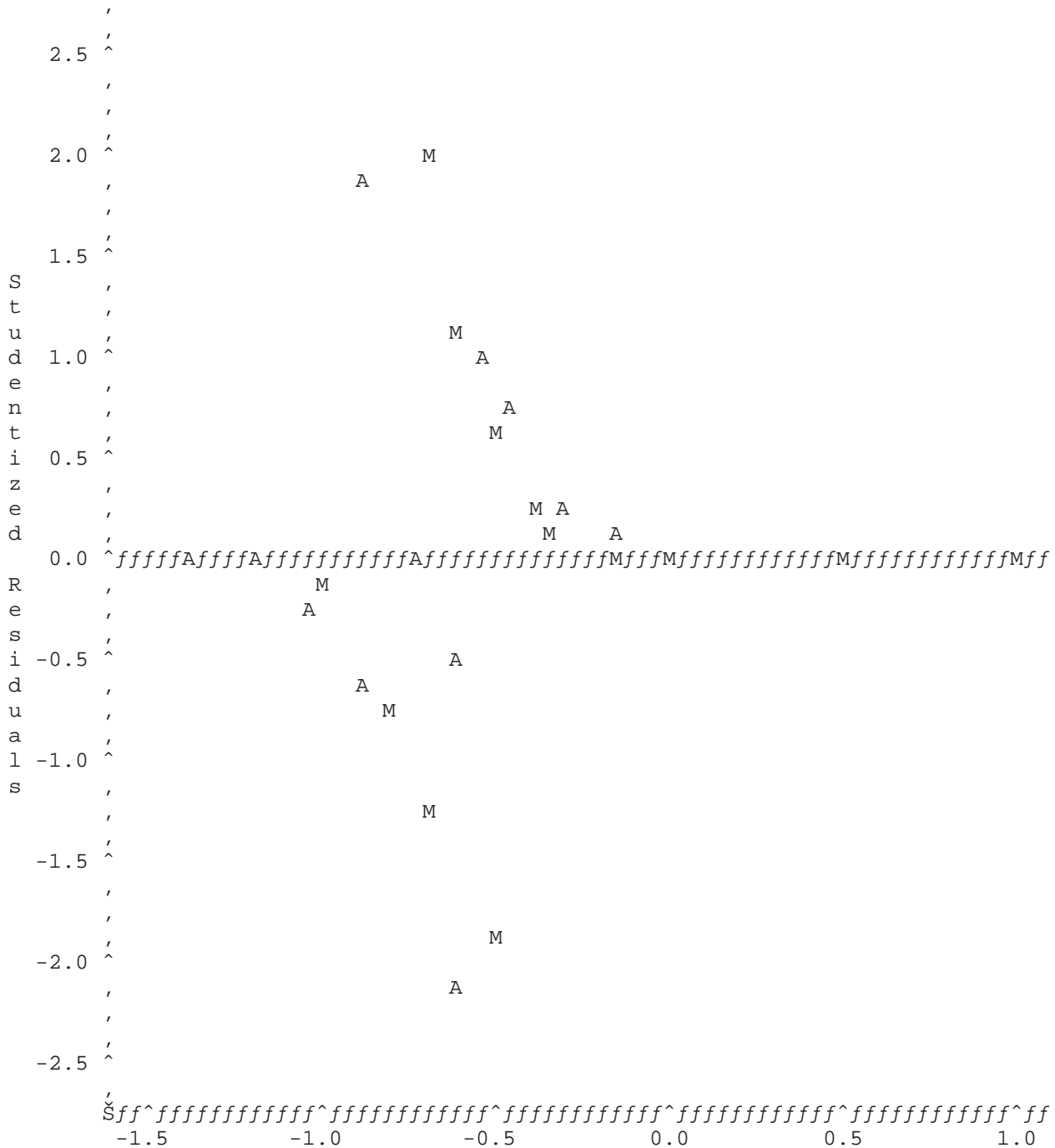
25	2	1.000	0.000	2	2	1.000	1.64485	1.99998
26	1	3.160	0.500	2	2	1.000	1.64485	2.00000
27	1	10.000	1.000	2	2	1.000	1.64485	2.00000

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
16	1.39258	0.74035	2.05656	0.37018	-0.33138
17	1.89998	1.31308	-0.50976	0.65654	0.40303
18	1.89998	1.31308	1.11847	0.65654	0.40303
19	2.21916	1.75965	-1.86317	0.87982	1.17411
20	2.21916	1.75965	0.58950	0.87982	1.17411
21	2.14907	1.94882	0.25189	0.97441	1.64485
22	2.06340	1.98689	0.12080	0.99344	1.64485
23	2.00203	1.99982	0.01313	0.99991	1.64485
24	2.00001	2.00000	0.00021	1.00000	1.64485
25	2.00001	2.00000	0.00021	1.00000	1.64485
26	2.00000	2.00000	0.00000	1.00000	1.64485
27	2.00000	2.00000	0.00000	1.00000	1.64485

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

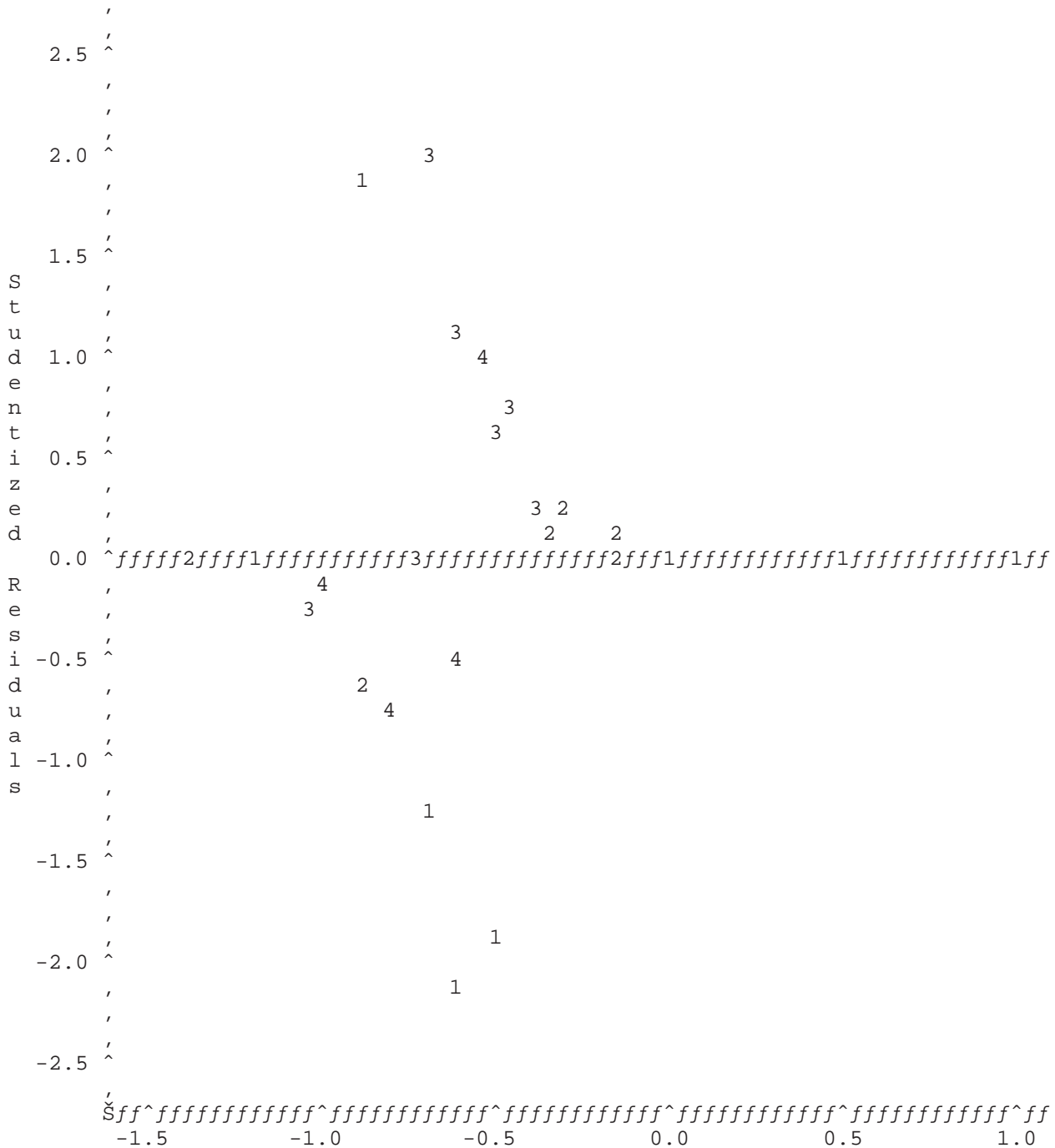
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS TREATMENT GROUP



11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS EXPERIMENTAL STAGE



11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=1 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.4180899	8	1.2838361	0.4539046	-2.1026241	1.8917429

----- Agent=VR Experimental Stage=2 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.0877265	8	0.2997577	0.1059804	-0.6032672	0.2179177

----- Agent=VR Experimental Stage=3 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.6392082	7	0.7782146	0.2941375	-0.2224905	2.0565634

----- Agent=VR Experimental Stage=4 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.0933126	4	0.7863351	0.3931675	-0.7713896	1.0174782

LD50 VR

8

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure
 Class Level Information

Class	Levels	Values
STAGE	4	1 2 3 4

Number of observations in by group = 27

LD50 VR

9

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS
 OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure

Dependent Variable: STUDRES		Studentized Residuals			
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	4.67668317	1.16917079	1.48	0.2411
Error	22	17.33341053	0.78788230		
Corrected Total	26	22.01009370			
R-Square		C.V.	Root MSE	STUDRES Mean	
0.212479		9999.99	0.887627	0.002025	

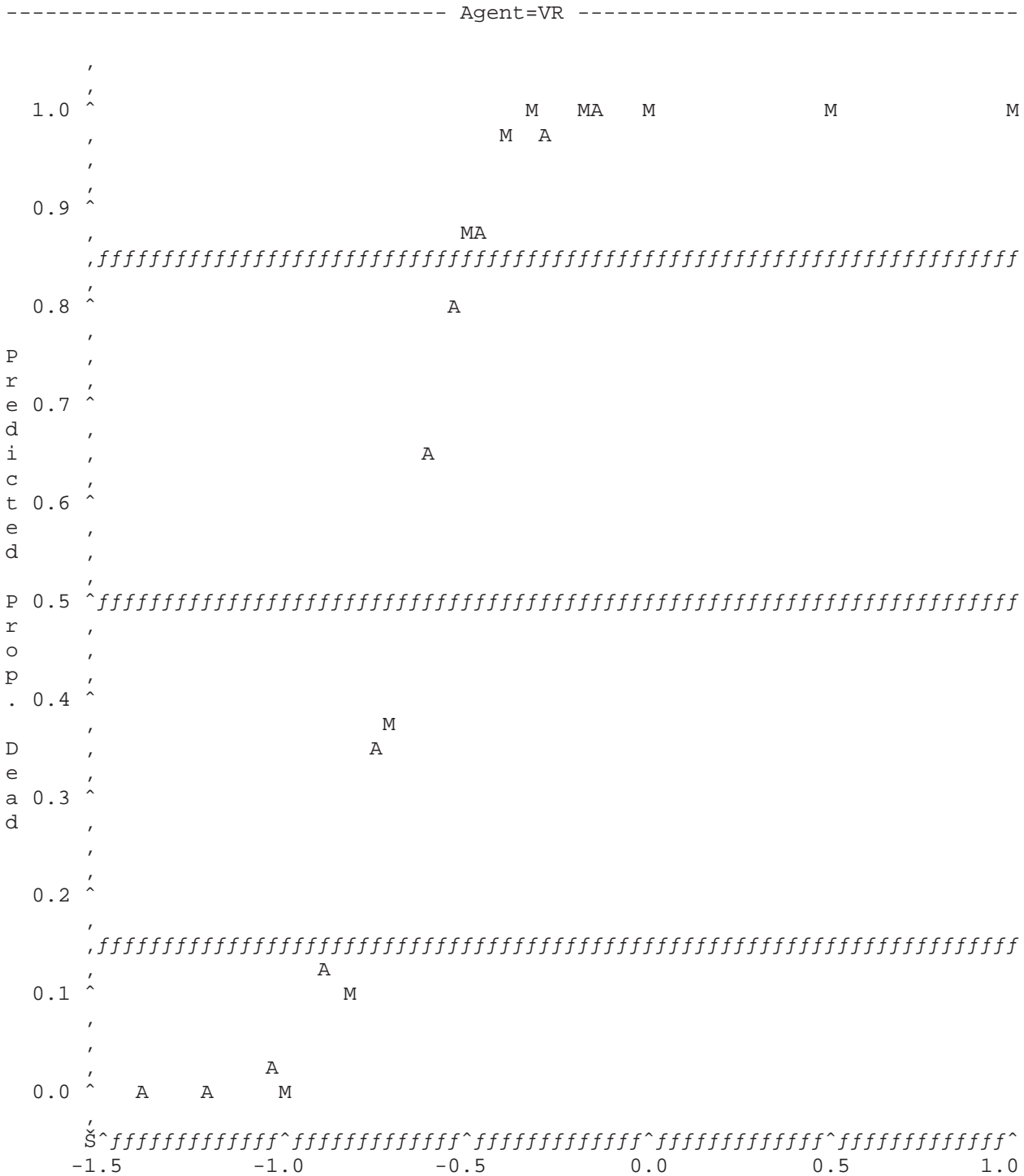
Source	DF	Type I SS	Mean Square	F Value	Pr > F
STAGE	3	4.35478879	1.45159626	1.84	0.1690
LOGDOSE	1	0.32189439	0.32189439	0.41	0.5293

Source	DF	Type III SS	Mean Square	F Value	Pr > F
STAGE	3	4.67256335	1.55752112	1.98	0.1469
LOGDOSE	1	0.32189439	0.32189439	0.41	0.5293

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBABILITY PLOT OF PREDICTED PERCENT DEAD WITH 16%, 50%, 84% REFERENCE LINES



11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT COEFFICIENTS AND COVARIANCE MATRIX FROM PROBIT REGRESSION

TRTGRP	SSE	RESIDSSQ	NTOT	NPTS	SLP	INT1	VARB1	COVB0B1	VARB0
AControl	18.3029	8.20476	27	12	5.51085	8.71240	3.82738	2.49790	1.74280
M291	16.2856	9.25862	32	15	7.57836	9.96566	8.42553	5.36013	3.53659

LD50 VR 12

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=AControl -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-1.09579	0.16869
VR	10	-1.28155	-0.90620	0.10867
VR	16	-0.99446	-0.85411	0.09393
VR	30	-0.52440	-0.76881	0.07354
VR	50	-0.00000	-0.67365	0.06134
VR	70	0.52440	-0.57850	0.06633
VR	84	0.99446	-0.49320	0.08313
VR	90	1.28155	-0.44110	0.09668
VR	99	2.32635	-0.25151	0.15487

Effective Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
0.08021	0.00738	0.12844
0.12411	0.02989	0.17221
0.13992	0.04348	0.18851
0.17029	0.07830	0.22415
0.21201	0.13743	0.29866
0.26394	0.19823	0.48419
0.32122	0.24248	0.84763
0.36216	0.26746	1.22351
0.56038	0.36221	4.90845

----- Agent=VR Treatment Group=M291 -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-0.96221	0.13341
VR	10	-1.28155	-0.82435	0.08602
VR	16	-0.99446	-0.78647	0.07428
VR	30	-0.52440	-0.72444	0.05786
VR	50	-0.00000	-0.65524	0.04752
VR	70	0.52440	-0.58605	0.05073
VR	84	0.99446	-0.52402	0.06364
VR	90	1.28155	-0.48614	0.07421

Effective Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
0.10909	0.01094	0.15654

0.14985	0.03804	0.19277
0.16351	0.05318	0.20565
0.18861	0.09027	0.23315
0.22119	0.15032	0.29057
0.25939	0.20647	0.43906
0.29921	0.24147	0.72242
0.32649	0.25962	1.00212

LD50 VR

13

11:01 Wednesday, February 1, 2006

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=M291 -----
(continued)

Agent	Perc- entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	99	2.32635	-0.34827	0.11985
Effective Dose for Percentile		Lower Confid- ence Bound	Upper Confid- ence Bound	
0.44847		0.32289	3.45151	

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
 PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
 RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----

Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
AControl	-0.67365	0.061340	-0.79388	-0.55343	0.21201	0.16074	0.27962
M291	-0.65524	0.047515	-0.74837	-0.56211	0.22119	0.17850	0.27409

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
 PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----

1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confidence Bound	Upper Confidence Bound
AControl	M291	-0.67365	-0.65524	0.018411	0.077591	1.04330	0.73508	1.48077

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----

Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
AControl	-0.67365	0.061340	-0.84620	-0.50110	0.21201	0.14249	0.31542
M291	-0.65524	0.047515	-0.78890	-0.52158	0.22119	0.16259	0.30090

11:01 Wednesday, February 1, 2006 17

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----

1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confidence Bound	Upper Confidence Bound
AControl	M291	-0.67365	-0.65524	0.018411	0.077591	1.04330	0.63117	1.72454

SAS ANALYSIS USING PROBSEPX PROGRAM FOR DELAYED DECON VR LD₅₀
Final Report After complete QC Audit of Data on 1 February 2006

File: VR All Delayed Decons SAS output 150622 Final ehb corrected 150623.doc

VR DELAYED DECONS

1

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Bleach delay -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD		
B1	B01	Weighted loss	
2.678177	1.514776	16.481614	

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD	Method: Gauss-Newton	B1	B01
Iter	Weighted loss	B1	B01
0	16.481614	2.678177	1.514776
1	14.167709	4.004550	-0.329207
2	13.440355	5.126522	-1.870909
3	13.334304	5.708301	-2.663551
4	13.330410	5.834224	-2.831595
5	13.330373	5.844848	-2.845079
6	13.330373	5.845633	-2.846079
7	13.330373	5.845689	-2.846149

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD		
---	--------------------------	--	--

Source	DF	Weighted SS	Weighted MS
Regression	2	83378.262198	41689.131099
Residual	16	6.763048	0.422691
Uncorrected Total	18	83385.025247	
(Corrected Total)	17	46617.187791	
Sum of Loss		13.330373	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval
			Lower Upper
B1	5.845688610	2.2145252356	1.1511281576 10.540249062
B01	-2.846149373	3.0655999379	-9.3448986303 3.652599885

Asymptotic Correlation Matrix

Corr	B1	B01
1		
B1	1	-0.991771078
B01	-0.991771078	1

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=RSDL delay -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD	
B1	B01	Weighted loss
2.411092	0.671269	25.853929

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD	Method: Gauss-Newton		
Iter	B1	B01	Weighted loss
0	2.411092	0.671269	25.853929
1	4.191118	-2.617595	21.570669
2	6.636639	-7.134064	18.808410
3	8.991863	-11.492413	17.727955
4	10.552169	-14.386735	17.490479
5	11.081201	-15.370210	17.472338
6	11.157216	-15.511784	17.472005
7	11.163447	-15.523397	17.472002
8	11.163905	-15.524251	17.472002

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD		
---	--------------------------	--	--

Source	DF	Weighted SS	Weighted MS
Regression	2	86569.666119	43284.833059
Residual	10	3.194512	0.319451
Uncorrected Total	12	86572.860631	
(Corrected Total)	11	67827.302969	
Sum of Loss		17.472002	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	11.16390470	4.4856335030	1.169227551	21.158581842
B01	-15.52425054	8.2909104346	-33.997666389	2.949165304

Asymptotic Correlation Matrix

Corr	B1	B01
ff		
B1	1	-0.99912799
B01	-0.99912799	1

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=Soap delay -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD	
B1	B01	Weighted loss
2.428674	1.923941	23.142678

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD	Method: Gauss-Newton		
Iter	B1	B01	Weighted loss
0	2.428674	1.923941	23.142678
1	2.856208	1.095452	22.018087
2	3.086899	0.749485	21.952760
3	3.129481	0.688813	21.951088
4	3.133663	0.683035	21.951071
5	3.134017	0.682548	21.951071

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics

Source	DF	Weighted SS	Weighted MS
Regression	2	199.24073942	99.62036971
Residual	17	10.11521117	0.59501242
Uncorrected Total	19	209.35595058	
(Corrected Total)	18	194.49325272	
Sum of Loss		21.95107082	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	3.134016570	1.1118329729	0.7882678676	5.4797652724
B01	0.682548343	1.5889541332	-2.6698320835	4.0349287699

Asymptotic Correlation Matrix

Corr	B1	B01
ffffffffffffffffffffffffffffffff		
B1	1	-0.98087078
B01	-0.98087078	1

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Bleach delay -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
1	2	2	0.301	1	0	0.000	-1.64485	-0.00000
2	2	5	0.699	2	0	0.000	-1.64485	-0.00205
3	2	10	1.000	2	0	0.000	-1.64485	-0.16364
4	3	10	1.000	1	0	0.000	-1.64485	-0.08182
5	1	15	1.176	1	0	0.000	-1.64485	-0.14378
6	2	15	1.176	2	1	0.500	-0.00000	-0.28756
7	3	22	1.342	3	1	0.333	-0.43073	0.49119
8	1	30	1.477	1	1	1.000	1.64485	0.50274
9	2	30	1.477	1	0	0.000	-1.64485	0.50274
10	3	30	1.477	1	1	1.000	1.64485	0.50274
11	3	38	1.580	3	3	1.000	1.64485	2.16924
12	1	45	1.653	1	1	1.000	1.64485	0.84651
13	3	45	1.653	1	1	1.000	1.64485	0.84651
14	1	60	1.778	1	1	1.000	1.64485	0.96238
15	1	75	1.875	1	1	1.000	1.64485	0.99128
16	1	90	1.954	1	1	1.000	1.64485	0.99794
17	1	105	2.021	1	1	1.000	1.64485	0.99949
18	1	120	2.079	1	1	1.000	1.64485	0.99986

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
1	0.00000	0.00000	-0.00000	0.00000	-1.64485
2	0.00239	0.00017	-0.01270	0.00008	-1.64485
3	0.25454	0.04545	-0.24399	0.02273	-1.64485
4	0.12727	0.02273	-0.16156	0.02273	-1.64485
5	0.47529	0.16575	-0.48465	0.16575	-0.97109
6	0.95057	0.33151	1.52846	0.16575	-0.97109
7	2.51177	1.50148	-0.69350	0.50049	0.00124
8	1.06694	0.78484	0.55339	0.78484	0.78864
9	1.06694	0.78484	-2.01860	0.78484	0.78864
10	1.06694	0.78484	0.55339	0.78484	0.78864
11	3.33606	2.75265	0.63606	0.91755	1.38877
12	1.08443	0.96547	0.19870	0.96547	1.64485
13	1.08443	0.96547	0.19870	0.96547	1.64485
14	1.02680	0.99459	0.07532	0.99459	1.64485
15	1.00688	0.99908	0.03041	0.99908	1.64485
16	1.00172	0.99983	0.01283	0.99983	1.64485
17	1.00044	0.99996	0.00532	0.99996	1.64485
18	1.00012	0.99999	0.00193	0.99999	1.64485

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=RSDL delay -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
19	1	5	0.699	3	0	0.000	-1.64485	-0.00000
20	1	10	1.000	1	0	0.000	-1.64485	-0.00000
21	1	15	1.176	2	0	0.000	-1.64485	-0.00000
22	1	30	1.477	3	0	0.000	-1.64485	-0.00124
23	2	45	1.653	4	0	0.000	-1.64485	-0.31429
24	1	60	1.778	3	1	0.333	-0.43073	-0.23309
25	2	60	1.778	1	0	0.000	-1.64485	-0.07770
26	2	70	1.845	4	3	0.750	0.67449	0.89080
27	2	80	1.903	4	2	0.500	-0.00000	1.88430
28	1	90	1.954	3	3	1.000	1.64485	2.01939
29	2	120	2.079	2	2	1.000	1.64485	1.94004
30	1	180	2.255	1	1	1.000	1.64485	0.99997

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
19	0.00000	0.00000	-0.00000	0.00000	-1.64485
20	0.00000	0.00000	-0.00000	0.00000	-1.64485
21	0.00000	0.00000	-0.00000	0.00000	-1.64485
22	0.00140	0.00008	-0.00858	0.00003	-1.64485
23	0.46887	0.07729	-0.36467	0.01932	-1.64485
24	1.73567	0.75129	0.41001	0.25043	-0.67314
25	0.57856	0.25043	-0.61458	0.25043	-0.67314
26	3.34595	2.11837	1.05908	0.52959	0.07425
27	4.23369	3.05900	-1.59344	0.76475	0.72166
28	3.39229	2.70584	0.71258	0.90195	1.29273
29	2.04556	1.99280	0.08846	0.99640	1.64485
30	1.00003	1.00000	0.00048	1.00000	1.64485

----- Agent=VR Treatment Group=Soap delay -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
31	2	2	0.301	1	0	0.000	-1.64485	-0.00321
32	2	5	0.699	2	0	0.000	-1.64485	-0.11392
33	3	5	0.699	1	0	0.000	-1.64485	-0.05696

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
31	0.00395	0.000370	-0.01907	0.000370	-1.64485
32	0.18078	0.033431	-0.19977	0.016716	-1.64485
33	0.09039	0.016716	-0.13546	0.016716	-1.64485

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=Soap delay -----
 (continued)

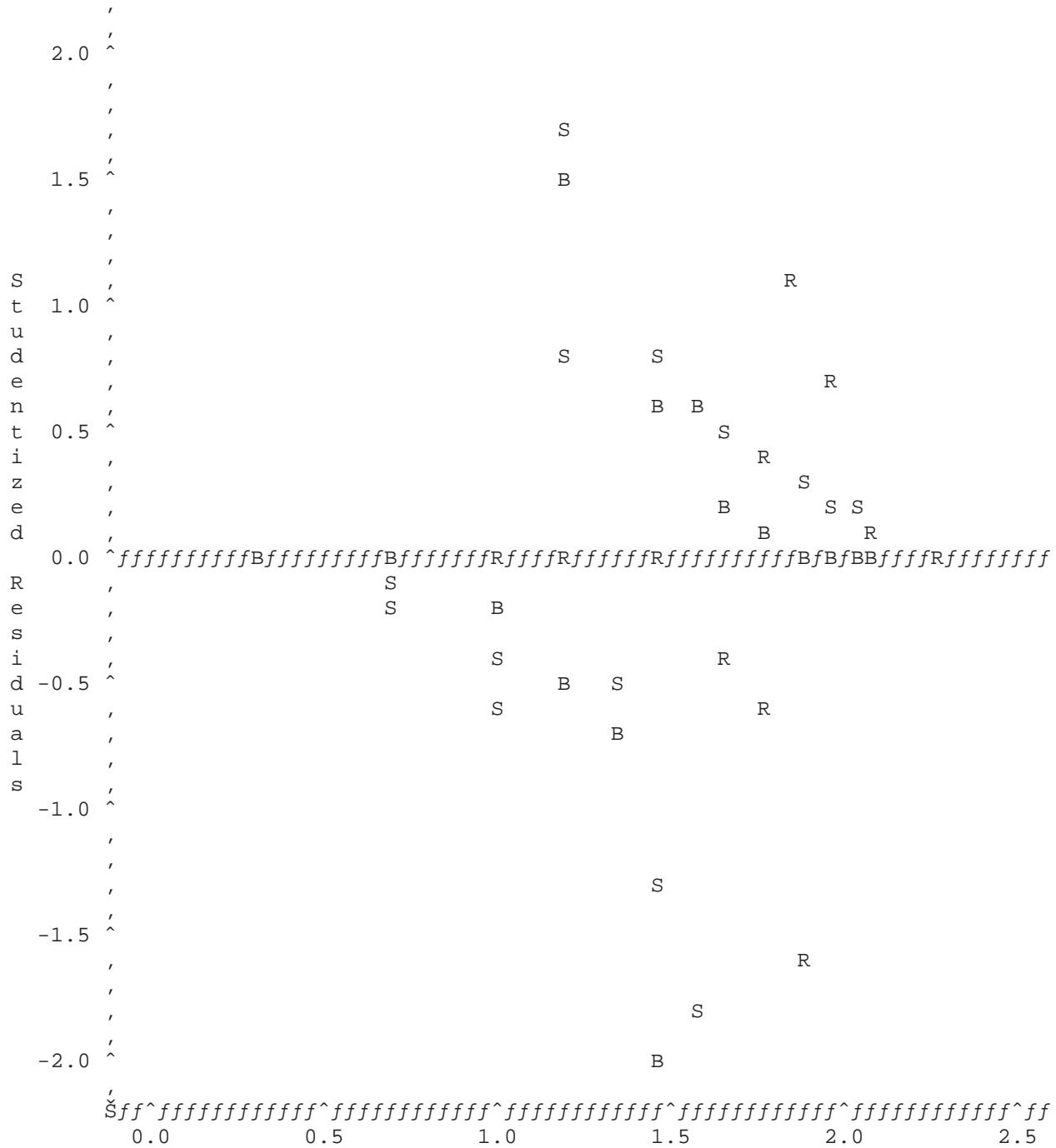
OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
34	2	10	1.000	2	0	0.000	-1.64485	-0.21741
35	3	10	1.000	1	0	0.000	-1.64485	-0.10871
36	1	15	1.176	1	1	1.000	1.64485	-0.01077
37	2	15	1.176	2	1	0.500	-0.00000	-0.02153
38	3	22	1.342	3	1	0.333	-0.43073	0.57460
39	1	30	1.477	1	0	0.000	-1.64485	0.36554
40	2	30	1.477	1	1	1.000	1.64485	0.36554
41	3	30	1.477	1	1	1.000	1.64485	0.36554
42	3	38	1.580	3	1	0.333	-0.43073	1.45201
43	1	45	1.653	1	1	1.000	1.64485	0.56451
44	3	45	1.653	1	1	1.000	1.64485	0.56451
45	1	60	1.778	1	1	1.000	1.64485	0.69614
46	1	75	1.875	1	1	1.000	1.64485	0.78813
47	1	90	1.954	1	1	1.000	1.64485	0.85156
48	1	105	2.021	1	1	1.000	1.64485	0.89505
49	1	120	2.079	1	1	1.000	1.64485	0.92495

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
34	0.69069	0.23664	-0.58732	0.11832	-1.18344
35	0.34534	0.11832	-0.38850	0.11832	-1.18344
36	0.53844	0.26384	1.74833	0.26384	-0.63156
37	1.07688	0.52767	0.83405	0.26384	-0.63156
38	2.16197	1.36828	-0.47438	0.45609	-0.11028
39	0.87932	0.62243	-1.32644	0.62243	0.31187
40	0.87932	0.62243	0.80462	0.62243	0.31187
41	0.87932	0.62243	0.80462	0.62243	0.31187
42	2.96899	2.21050	-1.79953	0.73683	0.63362
43	1.04776	0.80614	0.51235	0.80614	0.86374
44	1.04776	0.80614	0.51235	0.80614	0.86374
45	1.09449	0.89532	0.35944	0.89532	1.25530
46	1.09288	0.94050	0.26410	0.94050	1.55902
47	1.07770	0.96463	0.20005	0.96463	1.64485
48	1.06125	0.97815	0.15515	0.97815	1.64485
49	1.04715	0.98605	0.12269	0.98605	1.64485

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

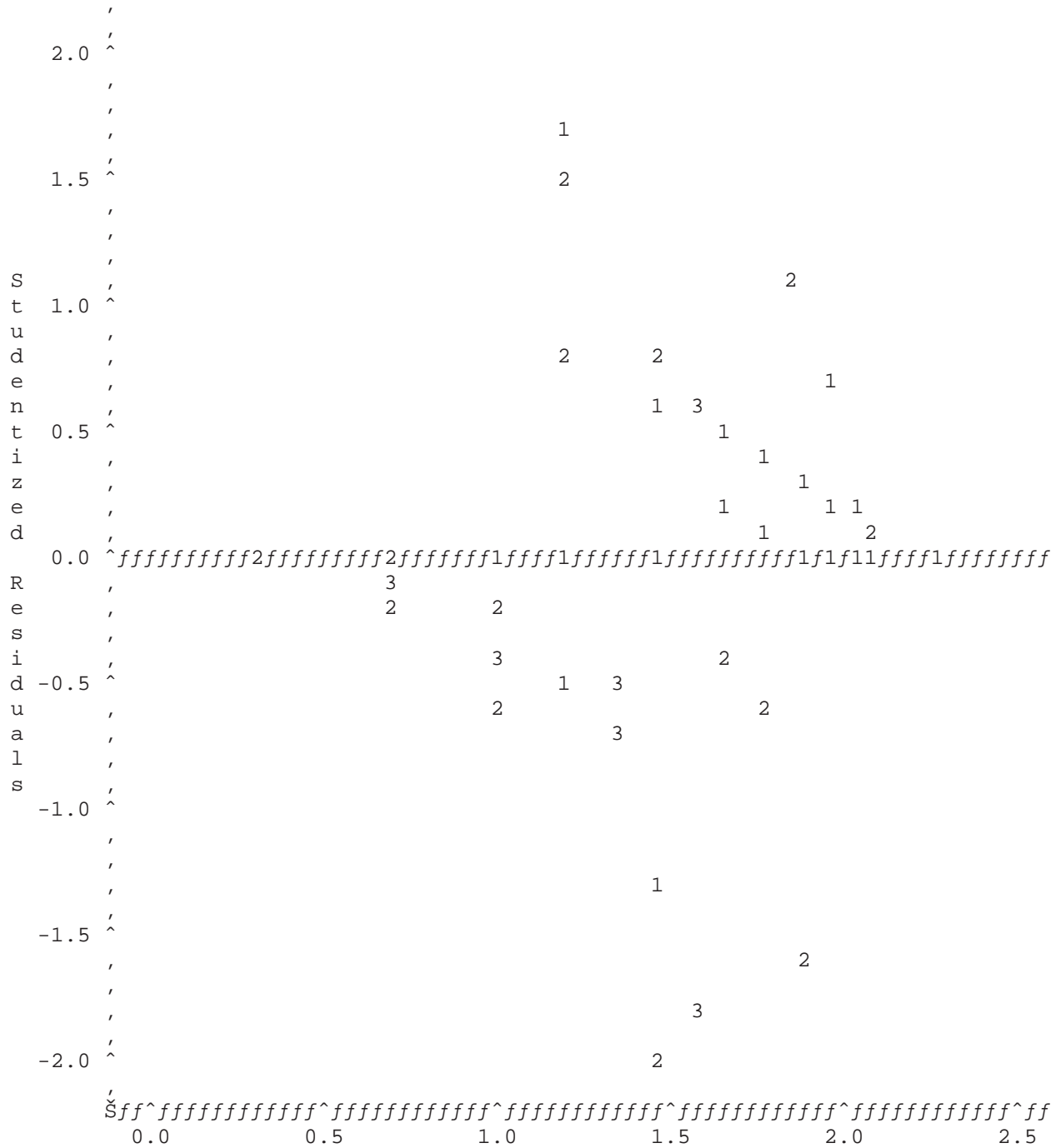
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS TREATMENT GROUP



14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS EXPERIMENTAL STAGE



14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=1 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.1540612	23	0.5254495	0.1095638	-1.3264365	1.7483326

----- Agent=VR Experimental Stage=2 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.0892992	15	0.9357391	0.2416068	-2.0185981	1.5284597

----- Agent=VR Experimental Stage=3 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.0861650	11	0.7561898	0.2279998	-1.7995315	0.8046226

10

14:40 Monday, June 22, 2015

VR DELAYED DECONS
SEPARATE-SLOPES DOSE-RESPONSE FITS
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure
Class Level Information

Class	Levels	Values
STAGE	3	1 2 3

Number of observations in by group = 49

11

14:40 Monday, June 22, 2015

VR DELAYED DECONS
SEPARATE-SLOPES DOSE-RESPONSE FITS
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure

Dependent Variable: STUDRES		Studentized Residuals			
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	0.74066281	0.24688760	0.46	0.7099
Error	45	24.02519752	0.53389328		
Corrected Total	48	24.76586032			
R-Square		C.V.	Root MSE	STUDRES Mean	
0.029907		2850.346	0.730680	0.025635	

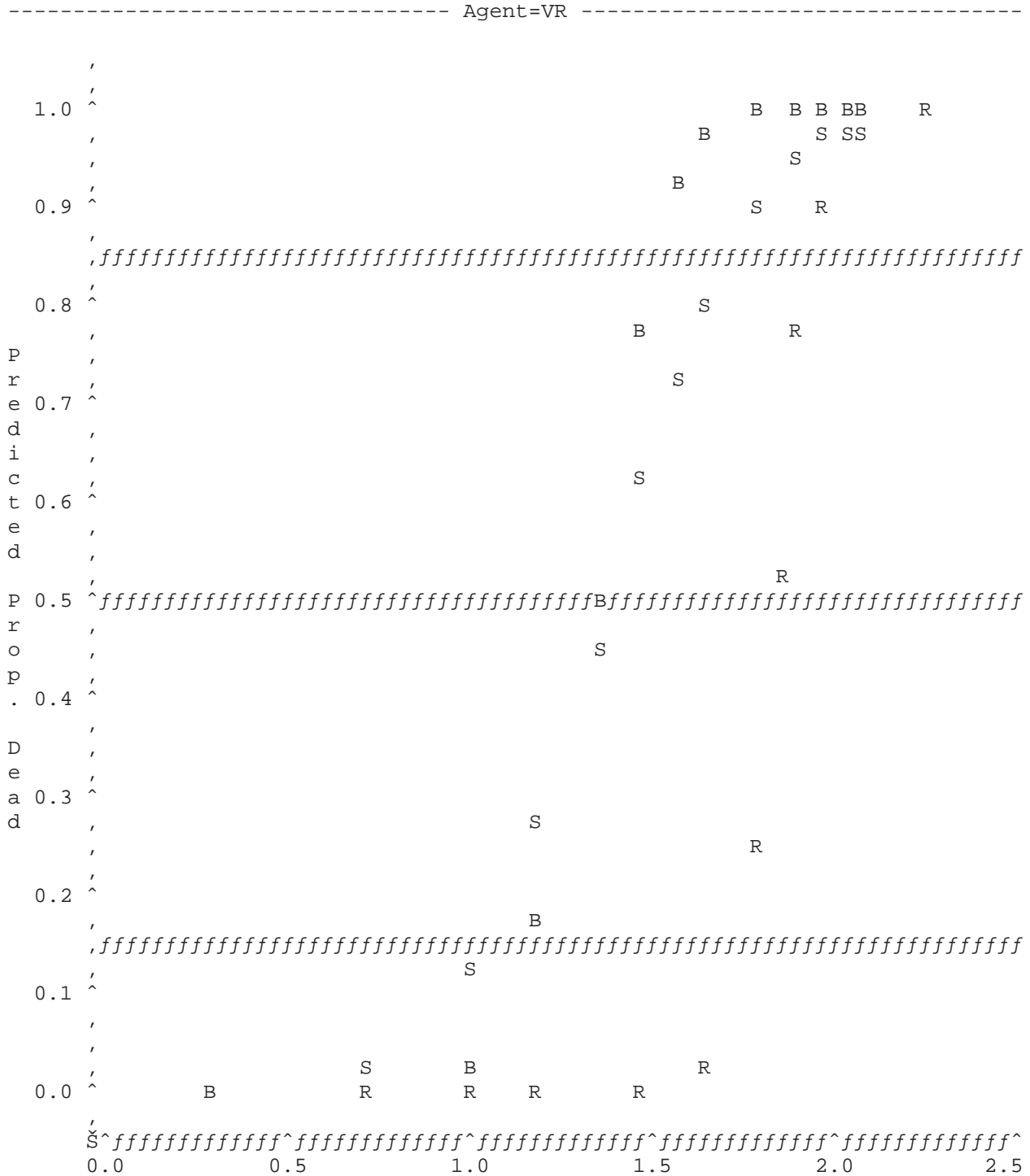
Source	DF	Type I SS	Mean Square	F Value	Pr > F
STAGE	2	0.71498529	0.35749264	0.67	0.5169
LOGDOSE	1	0.02567752	0.02567752	0.05	0.8274

Source	DF	Type III SS	Mean Square	F Value	Pr > F
STAGE	2	0.70133729	0.35066865	0.66	0.5234
LOGDOSE	1	0.02567752	0.02567752	0.05	0.8274

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBABILITY PLOT OF PREDICTED PERCENT DEAD WITH 16%, 50%, 84% REFERENCE LINES



VR DELAYED DECONS

13

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT COEFFICIENTS AND COVARIANCE MATRIX FROM PROBIT REGRESSION

		R						C	
		E						O	
T		S						V	V
R		I						B	A
T		D	N	N		I	A	0	R
G	S	S	T	P	S	N	R	B	B
R	S	S	O	T	L	T	B	B	B
P	E	Q	T	S	P	1	1	1	0

Bleach delay	13.3304	6.7630	25	18	5.8457	-2.8461	4.9041	-6.7330	9.3979
RSDL delay	17.4720	3.1945	31	12	11.1639	-15.5243	20.1209	-37.1576	68.7392
Soap delay	21.9511	10.1152	26	19	3.1340	0.6825	1.2362	-1.7329	2.5248

VR DELAYED DECONS

14

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S AND DELTA METHOD

----- Agent=VR Treatment Group=Bleach delay -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)	Effective Dose for Percentile
VR	1	-2.32635	0.94425	0.17573	8.7953
VR	10	-1.28155	1.12298	0.11607	13.2734
VR	16	-0.99446	1.17209	0.10147	14.8625
VR	30	-0.52440	1.25250	0.08117	17.8856
VR	50	-0.00000	1.34221	0.06814	21.9893
VR	70	0.52440	1.43192	0.07076	27.0345
VR	84	0.99446	1.51233	0.08542	32.5334
VR	90	1.28155	1.56144	0.09802	36.4285
VR	99	2.32635	1.74017	0.15448	54.9757

Lower Confid-ence Bound	Upper Confid-ence Bound	LCBD	UCBD
0.4802	14.243	3.9795	19.439
2.2801	18.783	7.8610	22.412
3.4614	20.483	9.4019	23.495
6.6790	24.231	12.3997	25.799
12.6344	32.166	16.1681	29.906
19.2768	52.940	19.6439	37.206
24.0223	96.969	22.1262	47.836
26.5711	145.130	23.4058	56.697
35.7041	676.291	27.3776	110.394

----- Agent=VR Treatment Group=RSDL delay -----					
Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)	Effective Dose for Percentile
VR	1	-2.32635	1.63007	0.092406	42.6644
VR	10	-1.28155	1.72365	0.058364	52.9241
VR	16	-0.99446	1.74937	0.049913	56.1525
VR	30	-0.52440	1.79147	0.038132	61.8692
VR	50	-0.00000	1.83845	0.031185	68.9362
VR	70	0.52440	1.88542	0.034689	76.8104
VR	84	0.99446	1.92753	0.044897	84.6302
VR	90	1.28155	1.95324	0.052854	89.7928
Lower Confid- ence Bound		Upper Confid- ence Bound	LCBD	UCBD	
6.5522		54.477	28.1158	64.741	
17.7479		62.555	40.6687	68.873	
23.2150		65.322	44.8271	70.339	
35.4921		71.189	52.0877	73.488	
53.0708		84.148	59.8859	79.354	
66.2947		119.061	65.6794	89.828	
73.2921		179.437	69.1077	103.639	
76.7883		233.933	70.7372	113.982	

14:40 Monday, June 22, 2015

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S AND DELTA METHOD

----- Agent=VR Treatment Group=RSDL delay -----
 (continued)

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)	Effective Dose for Percentile
VR	99	2.32635	2.04683	0.086177	111.385
Lower Confid-ence Bound		Upper Confid-ence Bound	LCBD	UCBD	
88.5334		631.094	75.4954	164.337	

----- Agent=VR Treatment Group=Soap delay -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)	Effective Dose for Percentile
VR	1	-2.32635	0.63532	0.28927	4.318
VR	10	-1.28155	0.96869	0.18261	9.305
VR	16	-0.99446	1.06030	0.15626	11.489
VR	30	-0.52440	1.21028	0.11982	16.229
VR	50	-0.00000	1.37761	0.09907	23.857
VR	70	0.52440	1.54494	0.11099	35.070
VR	84	0.99446	1.69492	0.14337	49.536
VR	90	1.28155	1.78653	0.16843	61.168
VR	99	2.32635	2.11990	0.27321	131.795
Lower Confid-ence Bound		Upper Confid-ence Bound	LCBD	UCBD	
0.0710		9.64	1.1704	15.933	
0.8339		16.05	4.0810	21.214	
1.6140		18.77	5.6758	23.258	
4.5531		25.34	9.4502	27.869	
12.1299		42.28	15.2560	37.306	
22.2792		102.32	21.2516	57.873	
31.0201		279.88	25.9369	94.607	
36.5568		537.48	28.6021	130.814	
61.4611		6246.02	38.4073	452.256	

SAS ANALYSIS USING PROBSEPX AND PRORATIO PROGRAMS FOR SERPACWA VR LD₅₀
Final Report (Experiments conducted by Battelle)

File: VR SERPACWA SAS output including 95 and 99.5 % CI 051103 ehb corrected 150604.doc

LD50 VR
12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

1

----- AGENT=VR TRTGRP=VRControl -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD		
B1	B01	Weighted loss	
2.960081	5.591638	33.016560	

Non-Linear Least Squares Iterative Phase			
Dependent Variable NDEAD	Method: Gauss-Newton		
Iter	B1	B01	Weighted loss
0	2.960081	5.591638	33.016560
1	4.472628	5.799306	28.035093
2	7.111566	6.147486	23.412263
3	12.664215	6.819788	18.155396
4	18.779945	7.536019	15.745045
5	22.471208	8.004751	15.328384
6	23.342233	8.146027	15.303489
7	23.452757	8.167565	15.302795
8	23.468636	8.170359	15.302784
9	23.469860	8.170616	15.302784
10	23.470064	8.170650	15.302784

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics	Dependent Variable NDEAD		
---	--------------------------	--	--

Source	DF	Weighted SS	Weighted MS
Regression	2	539.86788226	269.93394113
Residual	45	21.63732355	0.48082941
Uncorrected Total	47	561.50520581	

(Corrected Total)	46	561.35150602	
Sum of Loss		15.30278418	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	23.47006420	7.7065964176	7.9482322404	38.991896160
B01	8.17064966	1.0639898060	6.0276710920	10.313628233

Asymptotic Correlation Matrix

Corr	B1	B01
1		
B1	1	0.9408878658
B01	0.9408878658	1

LD50 VR

2

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS
PROBIT FITS TO DATA USING ALL EXPERIMENTAL STAGES, LOG10(DOSE)

----- AGENT=VR TRTGRP=VRSERPAC -----

Non-Linear Least Squares Grid Search	Dependent Variable NDEAD		
B1	B01	Weighted loss	
1.505377	4.430749	37.691247	

```

Non-Linear Least Squares Iterative Phase
Dependent Variable NDEAD Method: Gauss-Newton
Iter      B1      B01      Weighted loss
0         1.505377  4.430749  37.691247
1         1.706734  4.361467  37.394288
2         1.727433  4.359252  37.392009
3         1.727360  4.360060  37.391995
4         1.727472  4.360045  37.391996

```

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable NDEAD

Source	DF	Weighted SS	Weighted MS
Regression	2	116.80193376	58.40096688
Residual	46	67.88556439	1.47577314
Uncorrected Total	48	184.68749815	
(Corrected Total)	47	154.16402932	
Sum of Loss		37.39199555	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
B1	1.727471673	0.44257221746	0.8366226424	2.6183207032
B01	4.360045444	0.24555318443	3.8657739834	4.8543169042

Asymptotic Correlation Matrix

```

Corr      B1      B01
ffffffffffffffffffffffffffffffffffffffff
B1         1      -0.344023145
B01      -0.344023145      1
LD50 VR

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3

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=VRControl -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
1	1	0.09	-1.05	1	0	0.000	-1.64485	-0.00000
2	1	0.09	-1.05	1	0	0.000	-1.64485	-0.00000
3	1	0.09	-1.05	1	0	0.000	-1.64485	-0.00000
4	1	0.09	-1.05	1	0	0.000	-1.64485	-0.00000
5	1	0.16	-.796	1	0	0.000	-1.64485	-0.00000
6	1	0.16	-.796	1	0	0.000	-1.64485	-0.00000
7	1	0.16	-.796	1	0	0.000	-1.64485	-0.00000
8	1	0.16	-.796	1	0	0.000	-1.64485	-0.00000
9	2	0.17	-.770	1	0	0.000	-1.64485	-0.00000
10	2	0.17	-.770	1	0	0.000	-1.64485	-0.00000
11	2	0.17	-.770	1	0	0.000	-1.64485	-0.00000
12	2	0.17	-.770	1	0	0.000	-1.64485	-0.00000
13	2	0.19	-.721	1	0	0.000	-1.64485	-0.00000
14	2	0.19	-.721	1	0	0.000	-1.64485	-0.00000
15	2	0.19	-.721	1	0	0.000	-1.64485	-0.00000
16	2	0.19	-.721	1	0	0.000	-1.64485	-0.00000
17	3	0.31	-.509	1	0	0.000	-1.64485	-0.00000
18	3	0.31	-.509	1	0	0.000	-1.64485	-0.00000
19	3	0.31	-.509	1	0	0.000	-1.64485	-0.00000
20	3	0.31	-.509	1	0	0.000	-1.64485	-0.00000

21	3	0.50	-.301	1	0	0.000	-1.64485	-0.00051
22	3	0.50	-.301	1	0	0.000	-1.64485	-0.00051

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
1	0.00000	0.00000	-0.00000	0.00000	-1.64485
2	0.00000	0.00000	-0.00000	0.00000	-1.64485
3	0.00000	0.00000	-0.00000	0.00000	-1.64485
4	0.00000	0.00000	-0.00000	0.00000	-1.64485
5	0.00000	0.00000	-0.00000	0.00000	-1.64485
6	0.00000	0.00000	-0.00000	0.00000	-1.64485
7	0.00000	0.00000	-0.00000	0.00000	-1.64485
8	0.00000	0.00000	-0.00000	0.00000	-1.64485
9	0.00000	0.00000	-0.00000	0.00000	-1.64485
10	0.00000	0.00000	-0.00000	0.00000	-1.64485
11	0.00000	0.00000	-0.00000	0.00000	-1.64485
12	0.00000	0.00000	-0.00000	0.00000	-1.64485
13	0.00000	0.00000	-0.00000	0.00000	-1.64485
14	0.00000	0.00000	-0.00000	0.00000	-1.64485
15	0.00000	0.00000	-0.00000	0.00000	-1.64485
16	0.00000	0.00000	-0.00000	0.00000	-1.64485
17	0.00000	0.00000	-0.00000	0.00000	-1.64485
18	0.00000	0.00000	-0.00000	0.00000	-1.64485
19	0.00000	0.00000	-0.00000	0.00000	-1.64485
20	0.00000	0.00000	-0.00000	0.00000	-1.64485
21	0.00061	0.00005	-0.00640	0.00005	-1.64485
22	0.00061	0.00005	-0.00640	0.00005	-1.64485

LD50 VR

4

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=VRControl -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
23	3	0.50	-.301	1	0	0.000	-1.64485	-0.00051
24	6	0.63	-.201	1	0	0.000	-1.64485	-0.09880
25	6	0.63	-.201	1	0	0.000	-1.64485	-0.09880
26	6	0.63	-.201	1	0	0.000	-1.64485	-0.09880
27	6	0.63	-.201	1	1	1.000	1.64485	-0.09880
28	4	0.70	-.155	1	0	0.000	-1.64485	0.02630
29	4	0.70	-.155	1	0	0.000	-1.64485	0.02630
30	4	0.70	-.155	1	0	0.000	-1.64485	0.02630
31	4	0.70	-.155	1	0	0.000	-1.64485	0.02630
32	5	0.74	-.131	1	0	0.000	-1.64485	0.25232
33	5	0.74	-.131	1	1	1.000	1.64485	0.25232
34	5	0.74	-.131	1	0	0.000	-1.64485	0.25232
35	5	0.74	-.131	1	1	1.000	1.64485	0.25232
36	5	0.87	-.060	1	1	1.000	1.64485	0.84819
37	5	0.87	-.060	1	1	1.000	1.64485	0.84819
38	5	0.87	-.060	1	1	1.000	1.64485	0.84819
39	5	0.87	-.060	1	1	1.000	1.64485	0.84819
40	6	0.88	-.056	1	1	1.000	1.64485	0.87400
41	6	0.88	-.056	1	1	1.000	1.64485	0.87400
42	6	0.88	-.056	1	1	1.000	1.64485	0.87400
43	6	0.88	-.056	1	1	1.000	1.64485	0.87400

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
-----	-----	-----------------------	--------------------------	-------------------------	--------------------------

23	0.00061	0.00005	-0.00640	0.00005	-1.64485
24	0.22264	0.06192	-0.27225	0.06192	-1.53884
25	0.22264	0.06192	-0.27225	0.06192	-1.53884
26	0.22264	0.06192	-0.27225	0.06192	-1.53884
27	0.22264	0.06192	4.12448	0.06192	-1.53884
28	0.61570	0.32100	-0.72403	0.32100	-0.46491
29	0.61570	0.32100	-0.72403	0.32100	-0.46491
30	0.61570	0.32100	-0.72403	0.32100	-0.46491
31	0.61570	0.32100	-0.72403	0.32100	-0.46491
32	0.82854	0.54043	-1.13202	0.54043	0.10151
33	0.82854	0.54043	0.96265	0.54043	0.10151
34	0.82854	0.54043	-1.13202	0.54043	0.10151
35	0.82854	0.54043	0.96265	0.54043	0.10151
36	1.07189	0.96004	0.21272	0.96004	1.64485
37	1.07189	0.96004	0.21272	0.96004	1.64485
38	1.07189	0.96004	0.21272	0.96004	1.64485
39	1.07189	0.96004	0.21272	0.96004	1.64485
40	1.06419	0.96909	0.18559	0.96909	1.64485
41	1.06419	0.96909	0.18559	0.96909	1.64485
42	1.06419	0.96909	0.18559	0.96909	1.64485
43	1.06419	0.96909	0.18559	0.96909	1.64485

LD50 VR

5

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=VRControl -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
44	4	0.91	-.041	1	1	1.000	1.64485	0.93223
45	4	0.91	-.041	1	1	1.000	1.64485	0.93223
46	4	0.91	-.041	1	1	1.000	1.64485	0.93223
47	4	0.91	-.041	1	1	1.000	1.64485	0.93223

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
44	1.04062	0.98642	0.12057	0.98642	1.64485
45	1.04062	0.98642	0.12057	0.98642	1.64485
46	1.04062	0.98642	0.12057	0.98642	1.64485
47	1.04062	0.98642	0.12057	0.98642	1.64485

----- Agent=VR Treatment Group=VRSERPAC -----

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
48	1	0.09	-1.05	1	0	0.000	-1.64485	-0.016704
49	1	0.09	-1.05	1	0	0.000	-1.64485	-0.016704
50	1	0.09	-1.05	1	0	0.000	-1.64485	-0.016704
51	1	0.09	-1.05	1	0	0.000	-1.64485	-0.016704
52	1	0.16	-.796	1	0	0.000	-1.64485	-0.030129
53	1	0.16	-.796	1	0	0.000	-1.64485	-0.030129
54	1	0.16	-.796	1	1	1.000	1.64485	-0.030129
55	1	0.16	-.796	1	0	0.000	-1.64485	-0.030129
56	2	0.26	-.585	1	0	0.000	-1.64485	-0.035640
57	2	0.26	-.585	1	0	0.000	-1.64485	-0.035640
58	2	0.26	-.585	1	0	0.000	-1.64485	-0.035640

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
48	0.03113	0.007213	-0.08603	0.007213	-1.64485
49	0.03113	0.007213	-0.08603	0.007213	-1.64485
50	0.03113	0.007213	-0.08603	0.007213	-1.64485
51	0.03113	0.007213	-0.08603	0.007213	-1.64485
52	0.07405	0.021962	-0.15221	0.021962	-1.64485
53	0.07405	0.021962	-0.15221	0.021962	-1.64485
54	0.07405	0.021962	6.77822	0.021962	-1.64485
55	0.07405	0.021962	-0.15221	0.021962	-1.64485
56	0.13447	0.049413	-0.23243	0.049413	-1.64485
57	0.13447	0.049413	-0.23243	0.049413	-1.64485
58	0.13447	0.049413	-0.23243	0.049413	-1.64485

LD50 VR

6

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=VRSERPAC -----
(continued)

OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
59	2	0.26	-.585	1	0	0.000	-1.64485	-0.03564
60	2	0.39	-.409	1	0	0.000	-1.64485	-0.02496
61	2	0.39	-.409	1	0	0.000	-1.64485	-0.02496
62	2	0.39	-.409	1	0	0.000	-1.64485	-0.02496
63	2	0.39	-.409	1	0	0.000	-1.64485	-0.02496
64	3	0.51	-.292	1	0	0.000	-1.64485	-0.00501
65	3	0.51	-.292	1	0	0.000	-1.64485	-0.00501
66	3	0.51	-.292	1	0	0.000	-1.64485	-0.00501
67	3	0.51	-.292	1	0	0.000	-1.64485	-0.00501
68	3	0.75	-.125	1	0	0.000	-1.64485	0.04595
69	3	0.75	-.125	1	1	1.000	1.64485	0.04595
70	3	0.75	-.125	1	0	0.000	-1.64485	0.04595
71	3	0.75	-.125	1	0	0.000	-1.64485	0.04595
72	4	0.87	-.060	1	0	0.000	-1.64485	0.07250
73	4	0.87	-.060	1	1	1.000	1.64485	0.07250
74	4	0.87	-.060	1	0	0.000	-1.64485	0.07250
75	4	0.87	-.060	1	0	0.000	-1.64485	0.07250
76	4	2.10	0.322	1	0	0.000	-1.64485	0.27653
77	4	2.10	0.322	1	0	0.000	-1.64485	0.27653
78	4	2.10	0.322	1	0	0.000	-1.64485	0.27653
79	4	2.10	0.322	1	0	0.000	-1.64485	0.27653

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
59	0.13447	0.04941	-0.23243	0.04941	-1.64485
60	0.20315	0.08909	-0.31909	0.08909	-1.34638
61	0.20315	0.08909	-0.31909	0.08909	-1.34638
62	0.20315	0.08909	-0.31909	0.08909	-1.34638
63	0.20315	0.08909	-0.31909	0.08909	-1.34638
64	0.25717	0.12608	-0.38734	0.12608	-1.14512
65	0.25717	0.12608	-0.38734	0.12608	-1.14512
66	0.25717	0.12608	-0.38734	0.12608	-1.14512
67	0.25717	0.12608	-0.38734	0.12608	-1.14512
68	0.34617	0.19606	-0.50277	0.19606	-0.85578
69	0.34617	0.19606	2.06160	0.19606	-0.85578
70	0.34617	0.19606	-0.50277	0.19606	-0.85578
71	0.34617	0.19606	-0.50277	0.19606	-0.85578
72	0.38411	0.22831	-0.55340	0.22831	-0.74443
73	0.38411	0.22831	1.87052	0.22831	-0.74443

74	0.38411	0.22831	-0.55340	0.22831	-0.74443
75	0.38411	0.22831	-0.55340	0.22831	-0.74443
76	0.65706	0.46679	-0.95289	0.46679	-0.08333
77	0.65706	0.46679	-0.95289	0.46679	-0.08333
78	0.65706	0.46679	-0.95289	0.46679	-0.08333
79	0.65706	0.46679	-0.95289	0.46679	-0.08333

LD50 VR

7

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

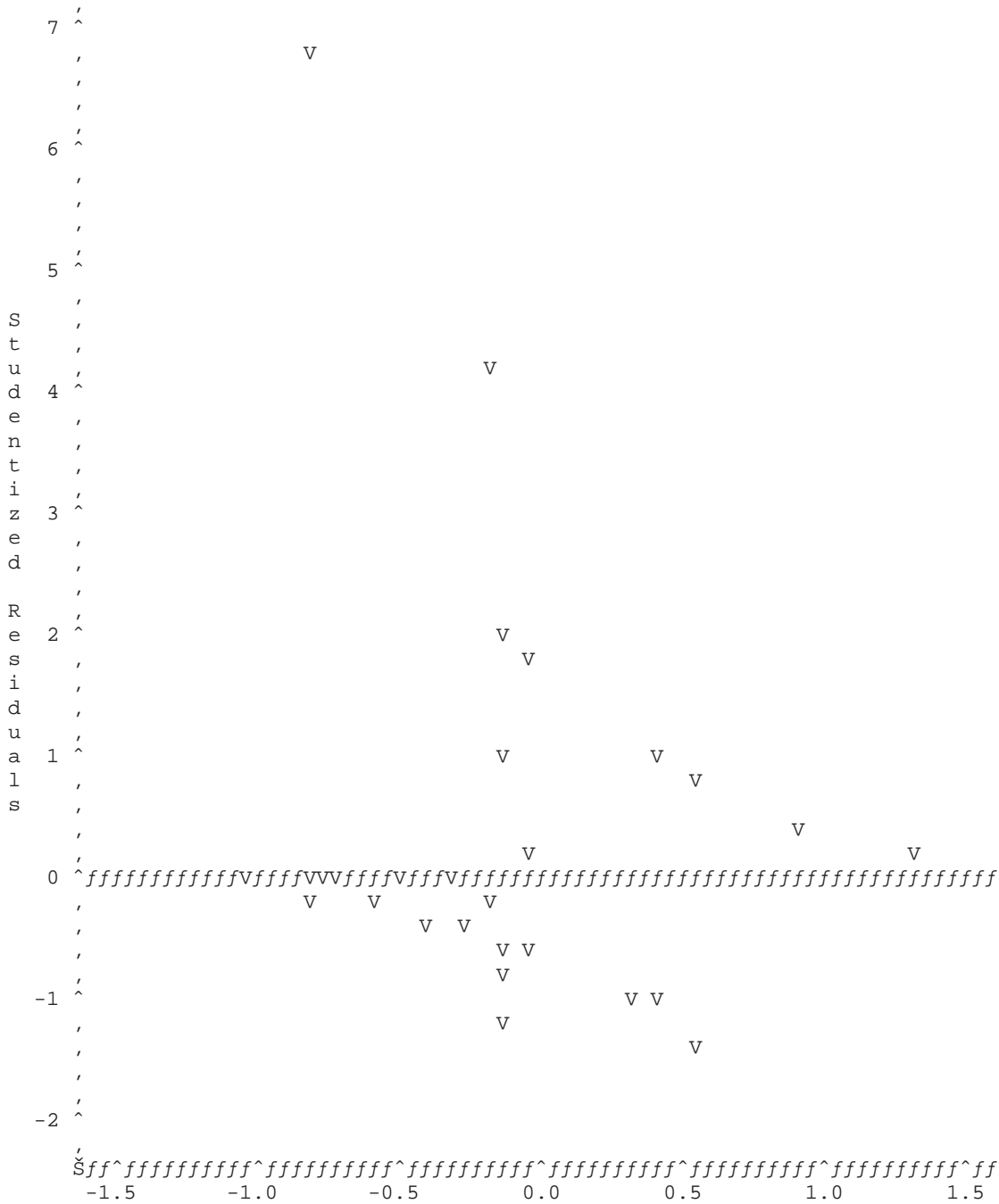
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

----- Agent=VR Treatment Group=VRSERPAC -----
(continued)

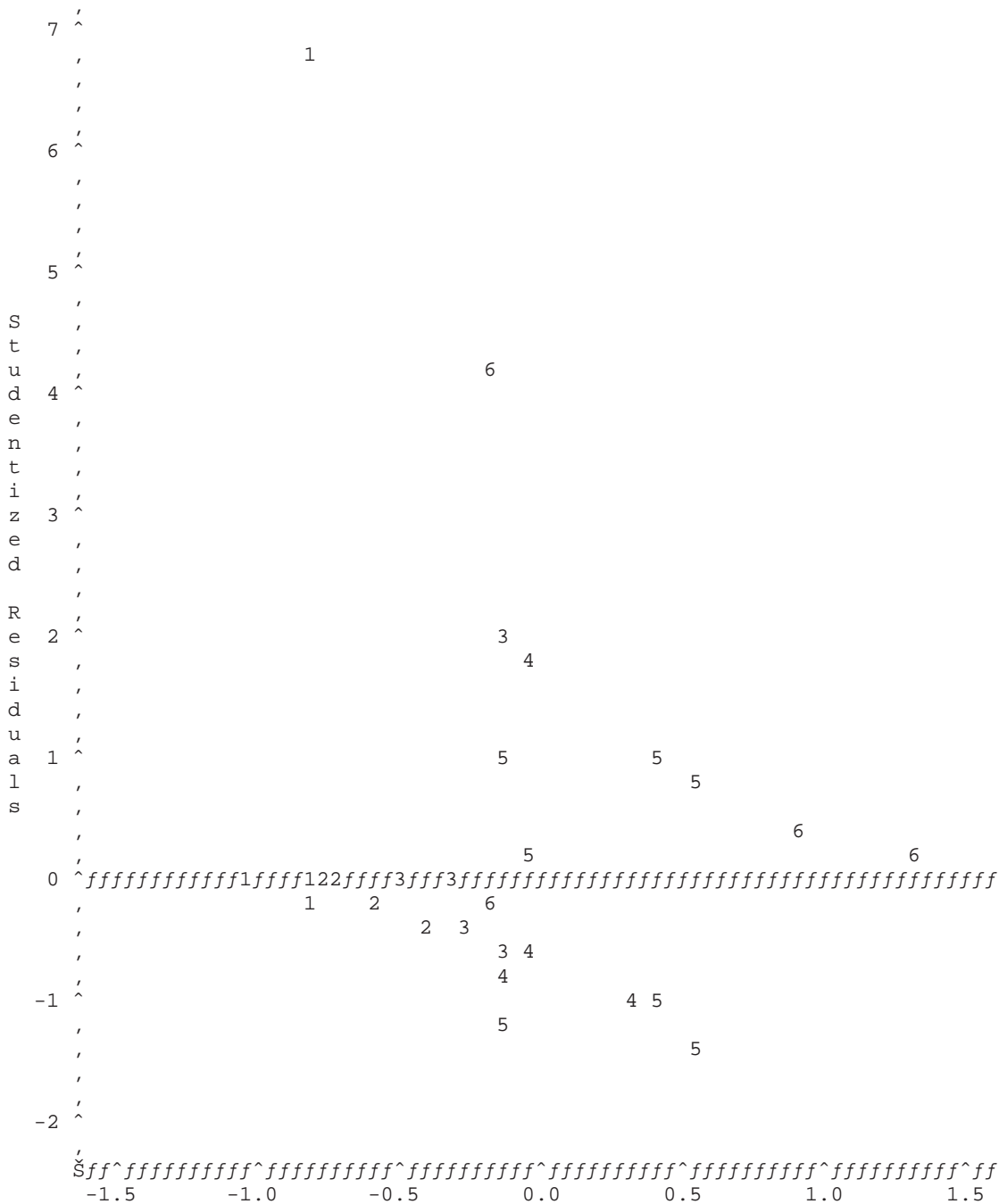
OBS	STAGE	Agent Dose (mg/kg)	Log10 Dose (mg/kg)	No. Animals	Observed N Dead	Prop. Dead	Probit of Percentile	LCL
80	5	2.50	0.398	1	1	1.000	1.64485	0.31994
81	5	2.50	0.398	1	0	0.000	-1.64485	0.31994
82	5	2.50	0.398	1	1	1.000	1.64485	0.31994
83	5	2.50	0.398	1	1	1.000	1.64485	0.31994
84	5	3.60	0.556	1	1	1.000	1.64485	0.41114
85	5	3.60	0.556	1	0	0.000	-1.64485	0.41114
86	5	3.60	0.556	1	1	1.000	1.64485	0.41114
87	5	3.60	0.556	1	0	0.000	-1.64485	0.41114
88	6	8.00	0.903	1	1	1.000	1.64485	0.61589
89	6	8.00	0.903	1	1	1.000	1.64485	0.61589
90	6	8.00	0.903	1	1	1.000	1.64485	0.61589
91	6	8.00	0.903	1	1	1.000	1.64485	0.61589
92	6	20.00	1.301	1	1	1.000	1.64485	0.82632
93	6	20.00	1.301	1	1	1.000	1.64485	0.82632
94	6	20.00	1.301	1	1	1.000	1.64485	0.82632
95	6	20.00	1.301	1	1	1.000	1.64485	0.82632

OBS	UCL	Predicted No. Dead	Studentized Residuals	Predicted Prop. Dead	Probit Pred. Pct Dead
80	0.71793	0.51893	0.98222	0.51893	0.04748
81	0.71793	0.51893	-1.05954	0.51893	0.04748
82	0.71793	0.51893	0.98222	0.51893	0.04748
83	0.71793	0.51893	0.98222	0.51893	0.04748
84	0.84069	0.62591	0.79258	0.62591	0.32104
85	0.84069	0.62591	-1.32612	0.62591	0.32104
86	0.84069	0.62591	0.79258	0.62591	0.32104
87	0.84069	0.62591	-1.32612	0.62591	0.32104
88	1.02660	0.82124	0.48400	0.82124	0.92011
89	1.02660	0.82124	0.48400	0.82124	0.92011
90	1.02660	0.82124	0.48400	0.82124	0.92011
91	1.02660	0.82124	0.48400	0.82124	0.92011
92	1.06574	0.94603	0.24755	0.94603	1.60754
93	1.06574	0.94603	0.24755	0.94603	1.60754
94	1.06574	0.94603	0.24755	0.94603	1.60754
95	1.06574	0.94603	0.24755	0.94603	1.60754

SEPARATE-SLOPES DOSE-RESPONSE FITS
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS TREATMENT GROUP



SEPARATE-SLOPES DOSE-RESPONSE FITS
OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
RESIDUALS VS. LOGDOSE - PLOTTING SYMBOL IS EXPERIMENTAL STAGE



LD50 VR

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 DESCRIPTIVE STATISTICS OF RESIDUALS BY STAGE

Analysis Variable : STUDRES Studentized Residuals

----- Agent=VR Experimental Stage=1 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.3735925	16	1.7089995	0.4272499	-0.1522062	6.7782170

----- Agent=VR Experimental Stage=2 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.1378802	16	0.1458757	0.0364689	-0.3190912	-5.98339E-48

----- Agent=VR Experimental Stage=3 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.0676833	15	0.6290612	0.1624229	-0.5027673	2.0616002

----- Agent=VR Experimental Stage=4 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
-0.3759425	16	0.7277049	0.1819262	-0.9528940	1.8705209

----- Agent=VR Experimental Stage=5 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.0832626	16	0.9408100	0.2352025	-1.3261191	0.9822231

----- Agent=VR Experimental Stage=6 -----

Mean	N	Std Dev	Std Error	Minimum	Maximum
0.4360179	16	1.0169186	0.2542297	-0.2722528	4.1244804

LD50 VR

11

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS
 ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure
 Class Level Information

Class	Levels	Values
STAGE	6	1 2 3 4 5 6

Number of observations in by group = 95

LD50 VR 12

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT DATA FROM PROC NLIN -- LISTING OF PREDICTED VALUES AND RESIDUALS

ANOVA OF RESIDUALS FOR STAGE EFFECTS

----- Agent=VR -----

General Linear Models Procedure

Dependent Variable: STUDRES		Studentized Residuals			
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	6	7.92927805	1.32154634	1.35	0.2444
Error	88	86.22384191	0.97981639		
Corrected Total	94	94.15311996			
	R-Square	C.V.	Root MSE	STUDRES Mean	
	0.084217	1862.271	0.989857	0.053153	

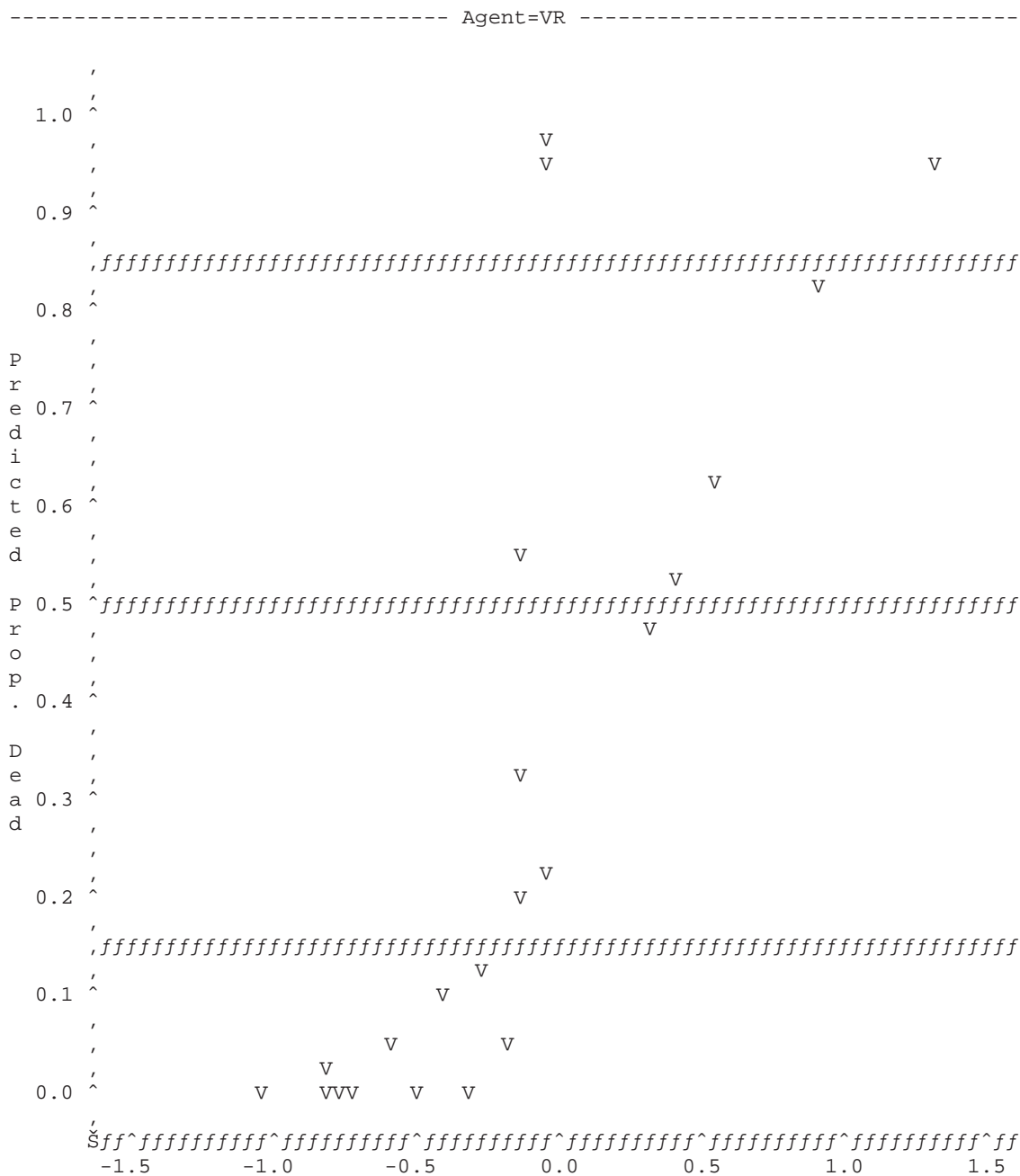
Source	DF	Type I SS	Mean Square	F Value	Pr > F
STAGE	5	7.75166458	1.55033292	1.58	0.1734
LOGDOSE	1	0.17761346	0.17761346	0.18	0.6713
Source	DF	Type III SS	Mean Square	F Value	Pr > F
STAGE	5	7.91850753	1.58370151	1.62	0.1640
LOGDOSE	1	0.17761346	0.17761346	0.18	0.6713

LD50 VR

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PROBABILITY PLOT OF PREDICTED PERCENT DEAD WITH 16%, 50%, 84% REFERENCE LINES



LD50 VR

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

OUTPUT COEFFICIENTS AND COVARIANCE MATRIX FROM PROBIT REGRESSION

TRTGRP	SSE	RESIDSSQ	NTOT	NPTS	SLP	INT1	VARB1	COVB0B1	VARB0
VRControl	15.3028	21.6373	47	47	23.4701	8.17065	59.3916	7.71504	1.13207
VRSERPAC	37.3920	67.8856	48	48	1.7275	4.36005	0.1959	-0.03739	0.06030

LD50 VR 15

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=VRControl -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-0.23421	0.037536
VR	10	-1.28155	-0.18970	0.024926
VR	16	-0.99446	-0.17746	0.021902
VR	30	-0.52440	-0.15744	0.017820
VR	50	-0.00000	-0.13509	0.015450
VR	70	0.52440	-0.11275	0.016356
VR	84	0.99446	-0.09272	0.019617
VR	90	1.28155	-0.08049	0.022339
VR	99	2.32635	-0.03597	0.034453

Effective Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
0.58316	0.37228	0.65042
0.64610	0.49143	0.69918
0.66456	0.52906	0.71499
0.69593	0.59358	0.74594
0.73267	0.66298	0.79610
0.77135	0.71742	0.87696
0.80775	0.75313	0.97783
0.83083	0.77164	1.05070
0.92051	0.83178	1.38315

----- Agent=VR Treatment Group=VRSERPAC -----

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	1	-2.32635	-0.97622	0.32744
VR	10	-1.28155	-0.37141	0.19638
VR	16	-0.99446	-0.20522	0.16767
VR	30	-0.52440	0.06689	0.13720
VR	50	-0.00000	0.37046	0.14118
VR	70	0.52440	0.67402	0.18203
VR	84	0.99446	0.94613	0.23506
VR	90	1.28155	1.11232	0.27119

Effective Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
0.1056	0.00617	0.295
0.4252	0.09020	0.837
0.6234	0.18132	1.159
1.1665	0.51445	2.182
2.3467	1.27455	5.710
4.7209	2.47376	19.076
8.8334	4.07651	61.839
12.9516	5.42380	129.331

LD50 VR

16

12:08 Thursday, November 3, 2005

SEPARATE-SLOPES DOSE-RESPONSE FITS

PERCENTILES WITH CONFIDENCE INTERVALS BASED ON FIELLER'S METHOD

----- Agent=VR Treatment Group=VRSERPAC -----
(continued)

Agent	Perc-entile	Probit of Percentile	Log(Eff. Dose) for Percentile	Std. Error of Log(Eff. Dose)
VR	99	2.32635	1.71714	0.41317
Effective Dose for Percentile		Lower Confid-ence Bound	Upper Confid-ence Bound	
52.1357		14.5618	1996.47	

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
 PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
 RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----

Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
VRControl	-0.13509	0.01545	-0.16537	-0.10481	0.73267	0.68332	0.78558
VRSERPAC	0.37046	0.14118	0.09375	0.64716	2.34670	1.24094	4.43776

12:08 Thursday, November 3, 2005 18

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
 ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL 95% C.I.
 PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----

1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confidence Bound	Upper Confidence Bound
VRControl	VRSERPAC	-0.13509	0.37046	0.50555	0.14202	3.20295	1.68730	6.08008

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
PERCENTILE ESTIMATES OF DOSES PRODUCING SPECIFIED RESPONSE
RATES SHOWN WITH DELTA-TYPE CONFIDENCE INTERVALS

----- Agent=VR Percentile=0.5 -----

Treatment Group	Log(Leth Dose) for Percentile	Standard Error for Log(L.D.)	Log (Lower Conf. Bnd)	Log (Upper Conf. Bnd)	Leth Dose for Percentile	Lower Confidence Bound	Upper Confidence Bound
VRControl	-0.13509	0.01545	-0.17855	-0.09163	0.73267	0.66290	0.80978
VRSERPAC	0.37046	0.14118	-0.02667	0.76759	2.34670	0.94043	5.85582

ICD CANDIDATE TREATMENTS FOR VR COMPARISONS AMONG LD50s
ESTIMATED BY SRT SLOPES PROBIT ANALYSES MODEL AT 99.5% CI
PROTECTIVE RATIOS AND CONFIDENCE BOUNDS FOR SPECIFIED PERCENTILES

----- Agent=VR Percentile=0.5 -----

1st Group (Denominator)	2nd Group (Numerator)	Log(L.D.), 1st Group	Log(L.D.), 2nd Group	Del(LogLD) 2nd - 1st	Std Err, Delta	Protective Ratio	Lower Confidence Bound	Upper Confidence Bound
VRControl	VRSERPAC	-0.13509	0.37046	0.50555	0.14202	3.20295	1.27658	8.03622